

The New England Journal of Medicine

Copyright, 1940, by the Massachusetts Medical Society

VOLUME 223

OCTOBER 3, 1940

NUMBER 14

PROTRUSION OF THE LOWER LUMBAR INTERVERTEBRAL DISKS*

WILLIAM JASON MIXTER, M.D.,† AND JOSEPH S. BARR, M.D.‡

BOSTON

THE first published report of a case operated on for protrusion of the intervertebral disk into the spinal canal with which we are familiar is that of Oppenheim and Krause¹ in 1909. Their case was one of a complete transverse lesion of the cauda equina at the third lumbar disk. The lesion was found at operation and removed, and the patient recovered. Middleton and Teacher² in England and Goldthwait³ in America reported cases in 1911. Numerous reports of so-called "enchondroma" appeared between that time and 1929. In the latter year Dandy⁴ reported 2 lumbar cases and recognized the distinct character of the lesion, comparing the extruded portion of the disk to the free fragments found in the knee joint and elsewhere. Peet and Echols⁵ also recognized the lesion. All these earlier reports had to do with cases showing more or less complete transverse lesions. Schmorl⁶ recognized protrusions from the disk margin as of common occurrence, but did not consider them of great neurological significance.

Our own interest was aroused by the case of a young man seen in 1932 with severe intractable sciatica following a fall. Neurologic signs were absent; nevertheless, this patient had a definite protrusion from the disk margin causing compression of the fifth lumbar root. This case and others impelled us⁷ to review our cases of enchondroma, and we found that about 75 per cent of the cases were not tumors but were protrusions of normal disk cartilage. In this paper, published in 1934, we called attention to the fact that unilateral leg pain was frequently the outstanding symptom. Since then a very considerable literature on the subject has accumulated. We shall not at-

tempt to enumerate these articles, but instead refer the reader to Saunders and Inman's⁸ review.

Protrusion of the intervertebral disk may occur at any level in the spinal canal, but it is only common in the lower two disks, that between the fourth and fifth lumbar vertebrae and that between the fifth lumbar and the sacrum. Over 90 per cent of the protrusions that caused symptoms occur in one or the other of these two disks. We propose to discuss only these lumbar cases.

An examination of the normal fourth lumbar intervertebral disk and the structures behind it reveals that the disk is shaped like a closed horseshoe and that the weakest point is laterally placed. The fifth lumbar root is far out to the side in its sheath. Ventral to the root is the posterior longitudinal ligament, with the disk margin in front of that structure. Posterior to it lie the outer margin of the ligamentum flavum and the inner lip of the articular facet arising from the fifth lumbar vertebra. The nerve lies in a bed of loose connective tissue. Any posterior displacement of or protrusion from the disk margin at this point tends to force the nerve back against the immovable margin of the articular facet (Fig. 1).

The extrusion is almost always laterally placed (Table 1). The extruded fragment is a hard, crumpled mass of fibrocartilage, usually lying free but sometimes attached to the disk margin. It may vary in size from a fragment 2 to 3 mm. in diameter up to a mass large enough to block completely the spinal canal. The mass may lie anterior to the posterior longitudinal ligament of the spine, or the ligament may have been split, allowing the mass to lie in direct contact with the dura. Rarely the extruded mass is soft and is surrounded by a certain amount of gelatinous material, probably from the nucleus.

We wish to emphasize at this point that a large proportion of the cases of sciatica recover spontaneously or under conservative orthopedic

*From the Neurosurgical Service and Orthopedic Service, Massachusetts General Hospital.

Read at the Fourth International Neurological Congress, Copenhagen, Denmark, August 24, 1939.

†Lecturer in neurosurgery, Harvard Medical School, chief of Neurological Service, Massachusetts General Hospital.

‡Instructor in orthopedic surgery, Harvard Medical School, assistant visiting orthopedic surgeon, Massachusetts General Hospital.

treatment. No patient should be investigated as a suspected case unless his symptoms have been severe and disabling and have persisted for months rather than weeks.

The symptoms and signs of protrusion of the

ening of the ligamentum flavum or arachnoiditis may give essentially the same clinical history and findings on physical examination as does protrusion of the posterior disk. This fact is of no great importance, however, as any two or all three of

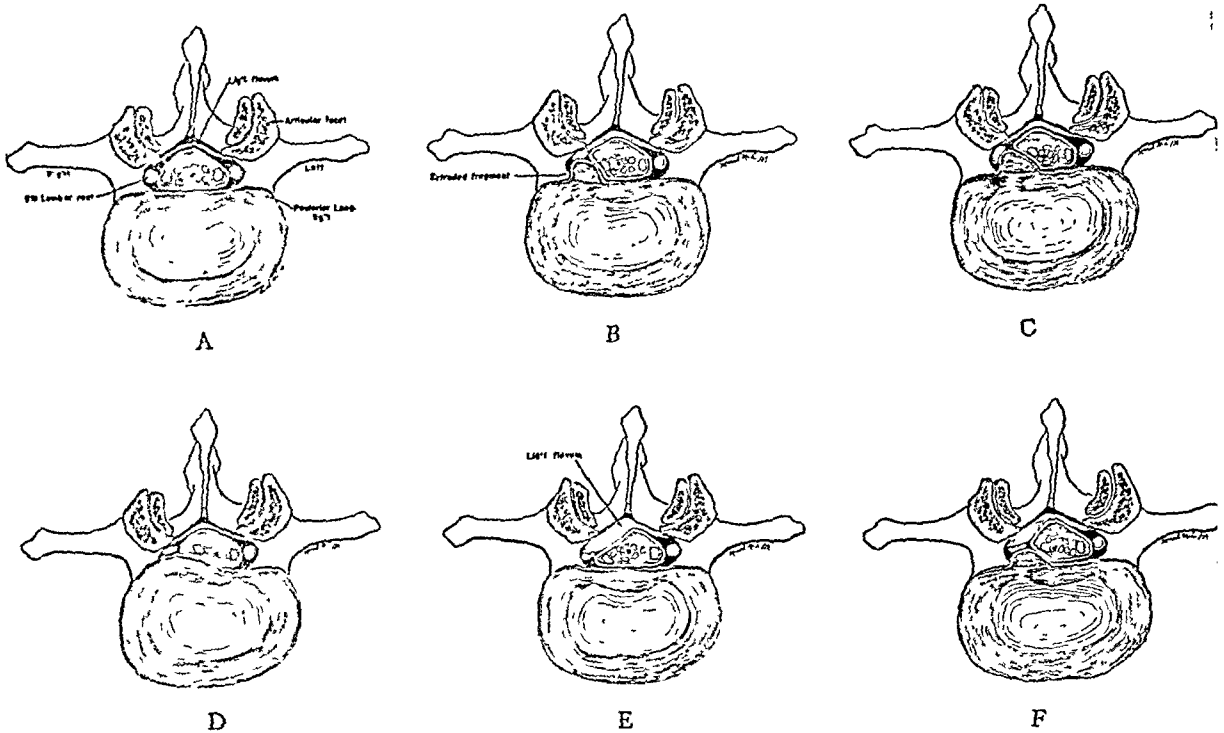


FIGURE 1. The Lumbar Intervertebral Disk and the Ligamentum Flavum.

A represents a section through a normal fourth lumbar disk; B, a free fragment of the disk, with compression of the fifth lumbar root; C, a free fragment, with lateral displacement of the fifth lumbar root; D, generalized posterior bulging of the disk; E, a thickening of the ligamentum flavum; F, a thickened ligamentum flavum, with an extended fragment of the disk.

fourth and the fifth lumbar disk are very similar (Table 2). Spurling and Bradford⁹ have analyzed their cases and believe that differentiation

TABLE 1. Incidence of Location and Character of Lesion in Relation to Anatomic Type.

Lesion	Incidence		
	Fourth Lumbar Disk	Fifth Lumbar Disk	Total
	%	%	%
Location			
Right	30	20	50
Left	22	18	40
Median	9	1	10
Character			
Free fragment	40	28	68
Attached fragment	12	8	20
Posterior bulge	9	3	12

is possible. So far we have been unable to achieve this result in our own cases. This matter is under investigation in various clinics, and it is to be hoped that their views will be confirmed. Thick-

these lesions may be present in the same case, as all of them demand surgical investigation. Rupture of the intervertebral disk probably occurs least ten times as frequently as do the other two together.

The protrusion may press straight back against the nerve root, or it may lie in the angle between the dural sac and the root sheath. More rarely there is no rent in the annulus but only a more or less generalized backward bulging of the annulus. The nerve lies just anterior and in close proximity to the articular facet arising from the vertebra below. This is invariably the position of the root as it crosses the intervertebral disk. A protrusion from or backward bulging of the disk margin tends to squeeze the root backward against the facet or against the ligamentum flavum.

The one outstanding symptom in these cases is pain—not a mild, sciatic pain but a severe,

tractable, disabling pain, which may have long remissions. Typically the pain runs down the back of the thigh and the outer side of the calf. Pain in the back may precede the leg pain, and a definite history of injury is given in about half the cases.

The one outstanding sign on physical examination is interference with straight leg-raising. This has been present in all our cases. Diminished or absent Achilles jerk occurs in 70 per cent, as does

TABLE 2. *Incidence of Traumatic Etiology, Symptoms and Physical Signs in Protrusion of the Fourth or Fifth Lumbar Disk (123 Cases).*

ETIOLOGY, SIGNS OR SYMPTOMS	INCIDENCE	
	%	%
Trauma		49
From lifting	22	
From other causes	27	
Leg pain		100
Thigh only	13	
Thigh and calf	66	
Thigh, calf and foot	21	
Back pain preceded by leg pain		48
Stiff lumbar spine		70
Loss of lumbar curve		47
List or scoliosis		37
Diminished straight leg raising		100
Diminished or absent ankle jerk		70
Sensory change (subjective or objective)		33

splinting of the lumbar spine. Loss of the lumbar curve, scoliosis and minor sensory changes are not uncommon. In severe cases motor weakness may be observed. Where the ruptured fragment is a large one, there may be evidence of compression of all the elements of the cauda equina with paralysis of the sphincters and so forth. This, however, is rare.

The total protein in the spinal fluid is usually somewhat increased (Fig. 2). Many cases show a level of 40 to 50 mg. per 100 cc., but in a very appreciable number the total protein, even in the first few drops drawn at the fifth lumbar space, is under 35 mg. Aside from this, the spinal fluid is generally normal.

We believe that the increased total protein in these cases is evidence of swelling and edema of the affected nerve roots above the point of compression. This condition has been noted many times at operation and can be demonstrated at times by examination with x-rays following Lipiodol injection. It may be that the serum protein in the swollen root passes through the arachnoid into the spinal fluid, thus raising the total protein.

The use of a contrast medium for x-ray examination of the spinal canal has been of inestimable value in the study of our cases, and in most of them we have employed Lipiodol (Fig. 3). This opaque

oil gives an excellent contrast, lies in a thin layer against the anterior dura, and can be moved about readily with the patient prone on the tip table. According to Hampton,¹⁰ it is by far the most satisfactory medium from the radiologist's point of view. We have long suspected that the occasional patient might give negative findings even with Lipiodol, and this has proved to be so in 2 cases. These patients were operated on notwithstanding a negative examination, and in each a ruptured fragment far to the side was found and removed.

The use of Lipiodol has certain disadvantages. It is so slowly absorbed that it may be considered a permanent foreign body. It is sufficiently irritating to cause considerable pain in the occa-

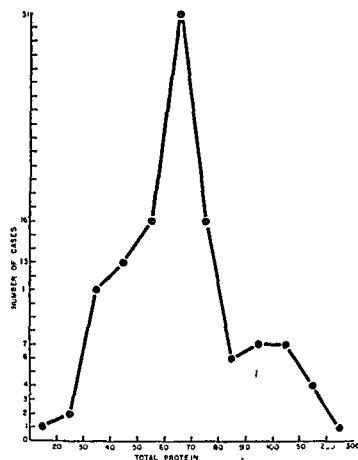


FIGURE 2. *Total Protein in the Spinal Fluid in Cases of Protruded Lumbar Intervertebral Disk.*

sional case. If the patient is tipped head down, either by accident or design, the Lipiodol may enter the cranium and become fixed there, occasionally causing severe intermittent headache. Lipiodol, therefore, is not used unless operative interference seems practically certain. In this we are in agreement with Love¹¹ and Camp,¹² who have handled a very large number of these cases. The Lipiodol is removed at operation, but this necessitates opening the dura, which would otherwise be unnecessary except in unusual cases.

The injection of air into the spinal canal gives satisfactory results in some cases (Fig. 4). We believe that Lipiodol will demonstrate a lesion in

some cases that would fail to be shown at all by injection of air. The contrast with air is poor, and the whole lumbar sac is filled, masking the defect, particularly if it be a small one. In some cases injection of air is used first. If it gives positive evidence of deformity of the lumbar sac, operation is indi-

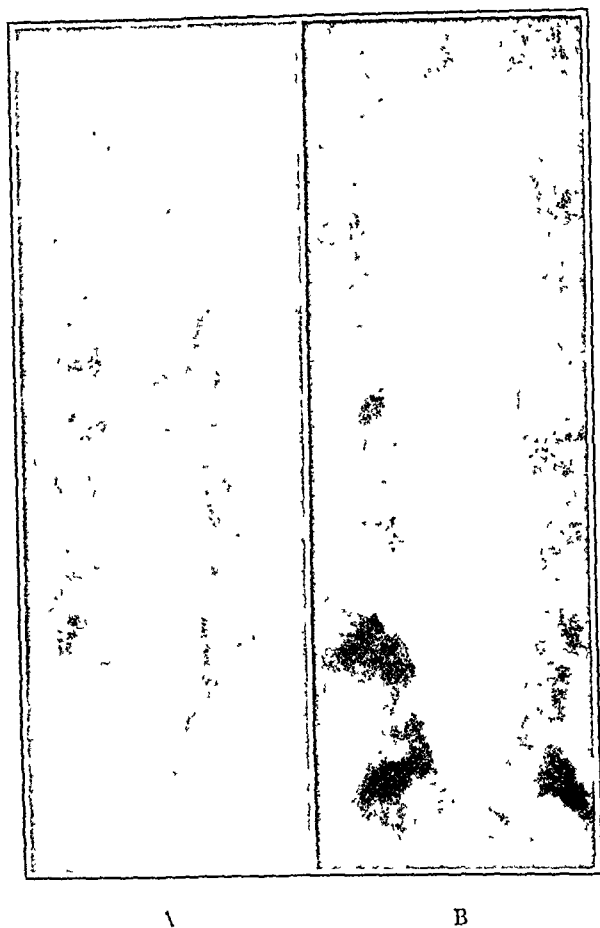


FIGURE 3. Defects as Shown by Lipiodol
In A there is a characteristic large defect, in B, a small filling defect of the right fifth-lumbar-root sheath.

cated; if, however, the examination is negative or unsatisfactory, it is checked by examination with Lipiodol a week later. We have not used Thorotrast, as we have believed that it is too dangerous. It may be that we are in error in this regard. It is to be hoped that some new contrast medium will be found which will be as satisfactory as Lipiodol, but which will be absorbed readily and will have no ill effects.

Spurling and Bradford⁹ suggest that typical cases may be operated on without any investigation with a contrast medium. This is possible in some cases, but they must be very carefully chosen. Under these circumstances it may be necessary to explore both the fourth and the fifth disks

on account of the similarity of the clinical pictures of each.

As already stated, rupture of the intervertebral disk is almost always at the fourth or fifth lumbar vertebra, and the symptom complex is constant. Notwithstanding this fact, a presumptive diagnosis of ruptured disk is often made on injection of Lipiodol carried out when such procedure is not warranted. The promiscuous use of Lipiodol for patients suffering from low back pain without the other signs enumerated above is dangerous and useless. The same is true of patients who have had symptoms for only a short time. The great majority recover spontaneously or under conservative orthopedic treatment. Investigation of the spinal canal for a ruptured disk should be reserved for those patients having severe, intractable sciatic pain accompanied by symptoms and signs strongly suggestive of the lesion. If this rule is followed, there will be fewer patients going about with Lipiodol in the lumbar sac or cranium.

Treatment of protruded disk may be operative, with removal of the fragment or stabilization of the spine by fusion, or may consist in non-operative measures such as rest in bed, or the use of a plaster jacket or some other form of corrective apparatus to hold the lumbar spine in flexion.

We realize fully that conservative measures or fusion will effect a symptomatic cure or temporary relief of symptoms in a certain number of the cases. We have no way of determining how many cases will be relieved or how many will recur, but we are of the opinion that the percentage in the latter will be large. Either of these forms of treatment requires a long period of immobilization. Operative removal seems far more logical, as the cause is definitely eliminated, the mortality is very low, and the period of disability is shorter than in the other methods of treatment.

Operative exposure of a protrusion may be carried out without the complete sacrifice of any lamina (Fig. 5). It is necessary only to cut away the lower edge of the lamina above and its upper edge below as advised by Fincher and Walker.¹¹ Adequate exposure of the laminae is essential. The ligamentum flavum is resected and the laminae cut away as stated above. If the lesion seems to be laterally placed, the inner edge of the articular facet arising from the vertebra below is trimmed off, the spinal canal is gently explored with the finger, and the lesion is demonstrated. If it is laterally situated, the dura and its contents are displaced medially, the compressed root displaced and the mass is exposed.

The posterior longitudinal ligament generally covers the mass, and it is necessary to split it before the disk cartilage is visible. In some cases the ligament has already been split, and the projecting mass lies in direct contact with the dura and root sheaths. The mass is lifted out if free or cut away if attached. An opening can usually be demonstrated, and an instrument passed into

operation. Lifting, driving an automobile or doing anything that may require a sudden strain is avoided for three months from the date of operation, and during this time muscle building exercises are continued. At the end of three months light work is permitted, and at the end of six, heavy work. In a few cases where the patient's work is particularly heavy, such as piano moving,

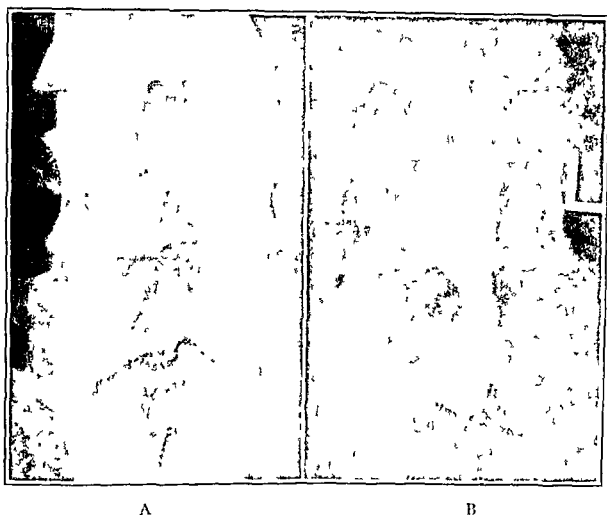


FIGURE 4 In Injection (A) and Lipiodol Injection (B) in the Same Patient

Note the sharp defect in the Lipiodol plate in contrast to the indistinct long defect in the air plate

the nucleus pulposus. Bleeding from the plexus of veins lying anterior to the root sheath may be brisk, and is controlled by cotton or muscle packs. If the lesion seems to be mesial, transdural resection is carried out. The Lipiodol should be removed in every case.

The aftercare of these patients is simple except where fusion has been combined with operative removal. Shells are not used. A simple dressing is all that is necessary, and the patient is moved freely. The wound is no more painful than is a laparotomy for gallstones, and the leg pain is generally relieved within a few days if not immediately. The patient is kept in bed about eighteen days and is then allowed to get up. A belt or brace may be used. Exercises to strengthen the back muscles are begun around this time, and the patient goes home about twenty-one days after

we have advised a change of occupation. A few patients have developed toe drop following operation, but this condition has never been permanent.

In our series one or more free fragments have been the most frequent finding, and break in continuity of the annulus with protrusion of an attached fragment of cartilage the second, while posterior bulging of the disk margin without a break in the annulus has been rare.

In the whole series, lesions of the fourth disk were commoner than those of the fifth. Thickening of the ligamentum flavum was encountered in association with protruded disk in 10 per cent of the cases, arachnoiditis in 3 per cent, and both in 1 per cent. It seems clear that this association points to a common cause—trauma. Sometimes the trauma results in protruded disk, sometimes in a thickened ligament, sometimes in arachnoiditis,

sometimes in a combination of two or all three of these lesions. But, as previously stated, protruded disk is by far the commonest of all. It may be that congenital weakness or degeneration of the annulus plays some part in the causation of this lesion and that the protrusion takes place at a weak spot.

We^{7, 14, 15} have reported our immediate results in previous papers, and further experience confirms our opinion that the operative risk is not great. Of 123 consecutive cases of rupture in the low lumbar region proved by operation, there

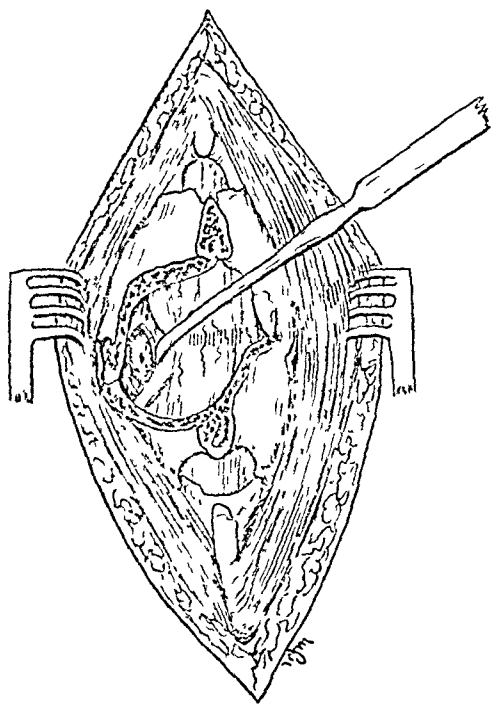


FIGURE 5. *Partial Laminectomy with Exposure of the Extruded Fragment.*

Note that neither lamina is cut across.

were 1 postoperative death and 1 case of later death from paraplegia, which was present preoperatively.

As regards the effect of operative removal of the extruded fragment, we have been able to trace 77 patients operated on over a year previously. We realize that one-year results may be too short to give accurate information. As reports of larger groups of cases with a longer elapsed period after operation are reported, some of our conclusions may have to be changed. The analysis of this group of cases is difficult, as the result must be measured largely by the personal estimate by the patient of the amount of his discomfort, and this estimate varies at different visits.

Thirty-six patients (47 per cent) are well and

complain of no residual discomfort. Some of our patients classified as well are working at less arduous jobs than the ones they held before they were ill. Twenty-five (32 per cent) are effective in their work or in other activities but do not class themselves as absolutely well. Many of these complain that their backs are tired after a hard day or that they have a little discomfort in their legs at times. A few have slight limitation of straight leg-raising or diminished ankle jerk. They are all satisfied that they are greatly improved. Thus 80 per cent of the results are good.

Eight (10 per cent) of the results are fair. These patients are able to work but are handicapped by pain if they do too much. They are satisfied that they have been definitely improved by the operation. The poor results (10 per cent) are as follows: Three patients have improved but are unable to work. They have interference with straight leg-raising, stiff back, loss of ankle jerk and so forth. Five have severe low back pain or recurrence of leg pain with the signs of protruded disk. One of these cases was re-explored, and a definite recurrence of the protrusion was found.

We are under the impression that the patients who had fusions performed at the time of laminectomy have shown slightly better results than those in whom no fusion was done. This difference is not great, and we can give a definite opinion on this point only after analysis of a larger group of cases than we have at present. Fusion following laminectomy or partial laminectomy adds to the length of the operation and the operative risk, and convalescence, of course, longer.

Although this series has been analyzed on the basis of one-year observations, a number of patients have been followed much longer, with results fully as good as those in the more recent group. We believe that it is correct to say that the results of operation in this disease are good in 80 per cent, fair in 10 per cent and poor in 10 per cent.

SUMMARY

Protrusion of the fourth or fifth lumbar intervertebral disk is a distinct entity. The rupture usually occurs at the side of the canal, with compression of the fifth lumbar or first sacral nerve root. Other roots may be affected as well.

The symptom complex is quite constant and is easily recognized. Sciatic pain, a stiff flat back, interference with straight leg-raising, absence of ankle jerk and elevation of the total protein in the spinal fluid are the most important features.

The diagnosis is confirmed by roentgenologi-

examination of the spinal canal following injection of a contrast medium

The operative treatment is described, and the results obtained are given.

REFERENCES

- Oppenheim H. and Krause F. Ueber Einklemmung bzw. Strangulation der Cauda equina. *Deutsche med. Wochenschr.* 35:697-700 1909
- Middleton G. S. and Tescher J. H. Injury of the spinal cord due to rupture of an intervertebral disc during muscular effort. *Glasgow M. J.* 76:16 1921
- Goldthwait J. E. The lumbosacral articulation: an explanation of many cases of lumbago, sciatica and paraplegia. *Boston M. & S. J.* 164:365-372 1911
- Dandy W. E. Loose cartilage from intervertebral disk simulating tumor of spinal cord. *Arch. Surg.* 19:660-672 1929
- Pett M. M. and Echols D. H. Herniation of nucleus pulposus cause of compression of spinal cord. *Arch. Neurol. & Psychiat.* 32:924-932 1934

- Schmorl G. Ueber Chordarreste in den Wirbelkörpern. *Zentralbl. f. Chir.* 55:2305-2310 1928
- Mixter W. J. and Barr J. S. Rupture of intervertebral disc with involvement of spinal canal. *New Eng. J. Med.* 211:210-215 1934
- Saunders J. B. de C. M. and Luman V. T. Intervertebral disc: critical and collective review. *Internat. Abstr. Surg.* 69:14-29 1939
- Spurling R. G. and Bradford F. K. Neurologic aspects of herniated nucleus pulposus at fourth and fifth lumbar interspaces. *J. A. M. A.* 113:19-20 1939
- Hampton A. O. personal communication
- Love J. C. Protruded intervertebral disks with note regarding hypertrophy of ligamenta flava. *J. A. M. A.* 113:2029-2034 1939
- Camp J. D. Roentgenologic diagnosis of intraspinal protrusion of intervertebral disks by means of radiopaque oil. *J. A. M. A.* 113:2024-2029 1939
- Fincher E. F. and Walker E. B. Sciatica and low back pain: study of thirty-one consecutive cases in which twenty-four were due to displaced intervertebral cartilage. *South. Surgeon.* 7:97-105 1938
- Barr J. S. Hampton A. O. and Mixter W. J. Pain low in the back and sciatica due to lesions of the intervertebral disks. *J. A. M. A.* 109:1265-1270 1937
- Mixter W. J. Rupture of the lumbar intervertebral disc: an etiologic factor for so-called sciatic pain. *Ann. Surg.* 106:777-787, 1937

ACUTE SURGICAL EMERGENCIES OF THE ABDOMEN IN PREGNANCY*

JUDSON A. SMITH, MD,† AND MARSHALL K. BARTLETT, MD‡

BOSTON

ANY acute abdominal condition which occurs in the nonpregnant woman may occur in the pregnant woman, with the possible exception of hemorrhage from a ruptured graafian follicle. There are several emergencies which can occur only in pregnant women, for example, incarceration of the retroverted pregnant uterus, rupture of the uterus and ectopic pregnancy. Since we wish to consider only emergencies arising during the course of an intrauterine pregnancy, we have excluded ectopic pregnancies and traumatic ruptures of the uterus during delivery. We have also excluded traumatic lesions of the other abdominal organs.

Table 1 shows a list of acute abdominal conditions and the number of cases of each encountered at the Boston Lying in Hospital from 1916 to 1938, inclusive. During this period there were 66,431 deliveries in and outside the hospital. The true incidence of these emergencies is undoubtedly higher than that shown in Table 1, because some cases were undoubtedly admitted to the surgical services of general hospitals.

There were no cases of acute pancreatitis. This condition has been reported as complicating pregnancy but it must be exceedingly rare, since it accounts for only about 1 per cent of all acute abdominal conditions, and furthermore is commoner in patients past forty. There were likewise no cases of perforation of an ulcer. Gastric or

duodenal ulcer being relatively uncommon in women as compared with men, the probability of a pregnant woman's having a perforated ulcer must be very small.

Biliary colic and acute cholecystitis are not so uncommon during pregnancy, but only rarely do they require immediate surgical intervention.

TABLE 1. Acute Abdominal Conditions in 66,431 Deliveries (1916-1938)

CONDITION	No. of Cases
Acute pancreatitis	0
Perforated ulcer	0
Acute gall bladder disease	3
Intestinal obstruction	1
Incarcerated hernia	1
Acute appendicitis	24
Ovarian cyst	10
Spontaneous rupture of uterus	14
Fibroid with acute degeneration or twisted pedicle	7
Incarcerated retroverted uterus	1
Total	61

Twenty-three of our patients had symptoms of gall bladder disease, but in only 3 were they severe or persistent enough to make operation necessary. Pregnancy does not materially interfere with either the diagnosis or the treatment of acute gall bladder disease.

The single case of intestinal obstruction occurred in the seventh month of pregnancy. The diagnosis was not made early. The patient had been vomiting for two days when admitted, was in poor condition, and died immediately after operation under local anesthesia. The immediate cause of death was asphyxia from aspiration of vomitus. Operation revealed an obstruction of the

*Read at the annual meeting of the Massachusetts Medical Society, Boston, May 21, 1940.

†Instructor in obstetrics, Harvard Medical School; assistant visiting obstetrician, Boston Lying in Hospital.

‡Assistant surgeon, Massachusetts General Hospital.

small bowel due to postoperative adhesions. This is the type of obstruction most likely to occur in pregnant women. In both nonpregnant and pregnant women the signs and symptoms of acute obstruction are the same, and there is the same urgent necessity of early diagnosis and operation. The earliest symptom of acute small-bowel obstruction is pain, usually severe and referred to the epigastric or umbilical regions. It often comes in spasms but may be continuous, particularly if the bowel is strangulated. Vomiting is an almost constant symptom, but its time of onset varies, so that it may not be an early one. Tenderness and distention are not early symptoms. Obstipation is inevitable, but the first enema may produce a good fecal result and it may be hours before the fact of obstipation can be established.

Hernia is a rare cause of acute abdominal emergencies in pregnancy. In this series there were 26 cases with ventral or umbilical hernias, none of which caused acute symptoms. There were 3 cases with inguinal hernias, one of which was incarcerated and required operation.

Acute appendicitis is by far the commonest abdominal emergency occurring in pregnant women. In this series the diagnosis of acute appendicitis was made in 24 cases, giving an approximate incidence of 1 in 2800 deliveries. In 3 cases the condition subsided spontaneously and the patients were not operated on. They all went to term without further attacks. One patient had an interval appendectomy two weeks after a subacute attack, with an uneventful recovery. Sixteen of the remaining 20 patients were operated on before rupture of the appendix had occurred, and all recovered. The question of the influence of drainage of the peritoneal cavity in causing abortion or premature labor is of interest, but it must be remembered that we are dealing with small groups of cases, and that the picture might be quite different if large numbers were available. In 11 of our 16 cases no drainage was used. Four of these 11 patients miscarried or delivered prematurely, while this occurred in 4 out of 5 of the unruptured but drained cases.

There remain 4 cases in which the appendix had ruptured. Three of these patients died and the fourth recovered after a long, stormy convalescence. Two cases were referred to the hospital by physicians in the seventh month of pregnancy, after several days of illness. Both patients showed at operation a ruptured appendix and general peritonitis. Both went into labor and both died. One patient, four months pregnant, was admitted after several days of mild pain in the right lower quadrant of the abdomen and

fever. These symptoms were not given the attention they deserved because on admission the patient was aborting. When, eight hours after the abortion was complete, the patient developed severe shock and upper abdominal pain, the diagnosis seemed very obscure. Forty-eight hours after admission, exploration revealed a ruptured appendix and general peritonitis. This patient had a long convalescence, complicated by a subdiaphragmatic abscess, but recovered. The fourth patient, who had severe cardiac disease, during the eighth month of her pregnancy was admitted with a history of epigastric pain, vomiting and diarrhea of two days' duration. The cardiac condition, plus the fact that labor started shortly after admission, diverted attention from the symptoms of appendicitis. She was delivered by cesarean section and died of general peritonitis on the eighth day. Autopsy revealed the source of the peritonitis as an abscess from a ruptured appendix.

Success in the treatment of acute appendicitis in the pregnant patient, as in the nonpregnant, depends on early diagnosis and operation before rupture of the appendix. The earliest symptom is pain, and typically it is first epigastric, shifting later to the right lower quadrant, but, as in the nonpregnant patient, this pattern may vary. The pain is not necessarily severe, and may be tolerated for some time before medical advice is sought.

Localized tenderness over the region of the appendix is probably the most consistent sign of appendicitis, and must never be ignored. In early pregnancy the appendix occupies its normal position and may, of course, extend down over the pelvic brim, so that a rectal examination should always be made. As the uterus increases in size, the cecum is forced upward and carries the appendix with it. Account of this must be taken in evaluating abdominal tenderness in pregnancy. Vomiting may be delayed or absent and involuntary spasm may not appear, even though the appendix is at the point of rupturing. It must be remembered that a physiologic leukocytosis occurs in pregnancy, so that the white-cell count may be 12,000 or 13,000, or even, rarely, as high as 16,000. The existence of a pregnancy should not deter one from an early operation, and needless to say, the pregnancy should not be interfered with.

Of the lesions which do not involve the uterus itself, ovarian cyst is second to appendicitis as a cause of acute abdominal emergencies. There were 10 such cases in this series, all of which were operated on successfully, except that 1 patient miscarried five days after operation. The diagnosis of ovarian cyst with twisted pedicle is generally easy, because the cyst can usually be felt if the

patient is examined carefully, under anesthesia if necessary. A cyst may be confused with a pedunculated fibroid, but if there are symptoms of strangulation the mistake is of no great practical importance. Sometimes in a well-advanced pregnancy a small cyst is situated so high that it can not be reached on vaginal examination and yet is not felt by abdominal palpation. X-ray examinations may be of great help in such a case, since many of the cysts complicating pregnancy are dermoids. Of 25 cases in which the nature of the cyst was known, it was a dermoid in 12.

Of the lesions that involve the uterus itself the commonest is spontaneous rupture. There were 14 cases in this series, 10 of which were those of patients with ruptures of cesarean scars. Of the other 4 cases, one was that of a patient with a bicornuate uterus, which ruptured during the fourth month, and the other ruptures occurred during prolonged labor. There was but 1 death, and that occurred in a case in which the rupture was not discovered. All the patients with rupture of a cesarean scar survived.

As a rule, when spontaneous rupture of the uterus occurs, the pain, the severe shock, the cessation of the fetal heart and sometimes the escape of the fetus into the abdominal cavity make the diagnosis easy. However, the pain may be very slight and may be obscured by labor pains, the bleeding may be negligible and shock absent, and the fetus may not escape through the rupture. Thus, it happens occasionally that when the abdomen is opened to perform a second section, a recent but entirely unsuspected rupture of the old scar is discovered. When such a symptomless rupture of the uterus occurs in a patient who is delivered vaginally, there is a grave abdominal emergency but little or no evidence of its existence. It may be diagnosed accidentally, as in a case (not included in this series) in which an extensive rupture of the lower segment just before normal delivery resulted in no change whatever in the patient's condition, and was discovered promptly only because the placenta escaped into the abdominal cavity; or such a rupture may be diagnosed only several days later when peritonitis has developed, or perhaps not until autopsy. Consequently, whenever a patient has been delivered vaginally who previously had a cesarean section, or whenever after vaginal delivery there is any reason whatsoever to suspect a rupture of the uterus, it is advisable to explore the uterus manually. In all cases of rupture of the uterus the treatment is immediate supravaginal hysterectomy.

Fibroids as a cause of acute abdominal emergencies during pregnancy ranked fourth in our series. There were 7 cases, in 4 of which the

fibroid was pedunculated. In 5 cases myomectomy was done, and in 2, hysterectomy. All the patients recovered without complications, but 2 went into premature labor following myomectomy, 1 in the seventh month and 1 in the eighth. Fibroids are a fairly common complication of pregnancy and the diagnosis is usually obvious. In most cases they are of little or no clinical significance. They seldom cause acute symptoms. In this series there were 147 cases with fibroids, 16 of which showed pain and tenderness. In 9 cases these symptoms were transient, subsiding with two or three days' rest in bed; in the other 7 the pain and tenderness were more severe and persisted. Most of the patients showed a moderate leukocytosis, but only 3 had fever, and the highest temperature was 100°F. The occurrence of pain and tenderness in fibroids during pregnancy is not usually a genuine abdominal emergency. If the tumors are pedunculated, reasonably prompt removal is advisable, but if not it is better to wait. In many cases the symptoms subside and the patient goes to term or to viability, whereas from 30 to 40 per cent of patients subjected to myomectomy miscarry.

Retroversion of the pregnant uterus very rarely requires operation, and still more rarely does it produce the picture of an acute abdominal emergency. In the 1 case reported here the patient was four months pregnant and was starting to miscarry when first seen. The angulation of the cervix resulted in obstruction. Severe lower abdominal pain and tenderness, slight bleeding, a rapid pulse and a very tender pelvic mass led to a preoperative diagnosis of a strangulated cyst or a ruptured ectopic pregnancy. At operation the retroverted, adherent uterus was easily freed and brought forward. It was then emptied by hysterotomy, a procedure the advisability of which is debatable in such cases.

SUMMARY

Any acute abdominal condition may occur in a pregnant woman that can occur in a nonpregnant one. The principles of recognizing and handling such conditions are the same in both groups. The prime necessity is not an immediate differential diagnosis but early recognition on the part of the general practitioner or obstetrician that an acute abdominal emergency may exist. He must maintain an attitude of suspicion with regard to abdominal pain. Persistent pain is the one early and almost invariable symptom of an acute abdominal emergency, and should receive immediate and thoughtful consideration. He must take care that the existence of a pregnancy does not in any way distract his attention from abdominal pain or lull his suspicions with regard to it.

SEVERE HEMORRHAGE FROM THE HEAD AND NECK

Its Management, with Report of a Case Showing the Retroparotid-Space Syndrome

HOLLIS L. ALBRIGHT, M.D.*

BOSTON

SERIOUS flooding hemorrhage from the head, mouth or deep vessels of the neck may often demand quick resourcefulness to avert impending disaster. When the hemorrhage is not readily controlled by pressure, packing, hemostat or primary ligation, the course of events may be rapid and the outcome fatal. Rarely does one encounter a hemorrhage beyond immediate surgical control, except from advanced intraoral cancer with sudden erosion of the large vessels of the floor of the mouth and neck, or from unusually severe and deep lacerations of the neck, such as those caused by fragments of glass from a shattered automobile windshield or by a deeply penetrating stab or bullet wound.

The resources of the physician for controlling such a hemorrhage are considerable. They may often prove useful in the salvage of patients outside of cancer institutions, where such hemorrhages more commonly occur. In the patient with extensive cancer of the deeper recesses of the mouth, pharynx, larynx or neck, hemorrhage ranks high among the terminal events. It has been well recognized that intraoral cancer rarely spreads beyond metastatic areas in the neck. Remote metastases to other organs have been found only in isolated cases, and practically never have they been regarded as a chief cause of death. Fatality usually results from locally destructive effects, namely, massive necrosis of tissue and slough of the floor of the mouth and neck, ischemic degeneration and ulceration of the metastatic cervical nodes, with secondary streptococcal infection ending in terminal septicemia, hemorrhage, progressive inanition, terminal pneumonia or any combination of these. There is also the possibility of radiation necrosis in the regions of the large blood vessels. One may be confronted with any of these complications in managing a patient at home, particularly during intervals following radiation treatment.

More often in cancer institutions does one become expectant of, and experienced in, meeting sudden massive hemorrhage from the head, neck or mouth. External hemorrhage from the head or neck may be directly controlled by the use

of hemostat, suture ligation or pressure by moist gauze packing, with supplementary proximal ligation of the major vessels if required. Bleeding from the mouth, pharynx or larynx, however, is not so directly controlled. It calls for effective indirect emergency measures, which are discussed herewith.

When a sudden, unheralded and massive effusion of blood appears at the mouth the difficulties

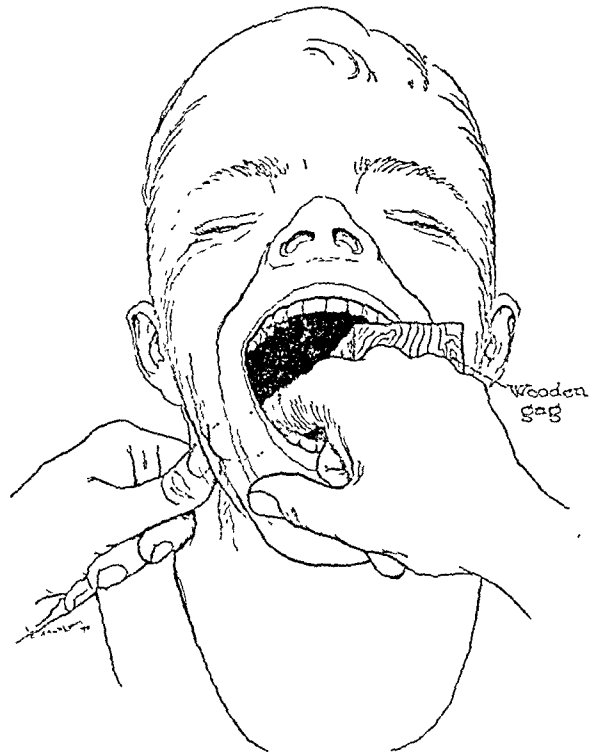


FIGURE 1. The First Stage in Attempting to Control Sudden Severe Hemorrhage from the Mouth and Pharynx: Intraoral and extraoral digital pressure.

are extreme, and unless a physician happens to be at hand, death soon occurs. Not infrequently, however, such premonitory signs as a previous, less severe hemorrhage or a slow trickling ooze may give warning of the likelihood of more serious, sudden hemorrhage. This allows the physician opportunity to consider the advisability of early proximal ligation of the affected vessel. This usually means ligation of either the external or, less often the internal, carotid artery, or control

*Assistant in surgery, Boston University School of Medicine; visiting surgeon, Massachusetts Memorial Hospitals, Boston.

of both by ligation of the common carotid artery. In any event, further preparation for an emergency should be made by having at the bedside a set for emergency tracheotomy, a wooden gag to insert between the teeth to prevent biting, sterile albolene, mineral oil or olive oil, a 2-inch-wide gauze strip for tight packing of the oropharynx and a small suction apparatus for aspiration of obstructing blood from the trachea and bronchial airways.

When one is suddenly confronted with bleeding from the mouth, temporary control may be attempted, first by insertion of a wooden gag between the teeth. The index finger can then be safely inserted deep along the lateral wall of the pharynx, firm to hard counterpressure being applied at the same time over the carotid vessels in the neck with the thumb or with the fingers of the opposite hand (Fig. 1). Such digital pressure may be shifted quickly to the opposite wall, and in certain cases this helps to indicate the source of the hemorrhage, and to allow time for the orderly execution of measures for more permanent control.

This temporary procedure suffices only with moderate hemorrhage, and in such a case it may be worth while to maintain such pressure for a prolonged period in an attempt to induce spontaneous clotting. In the presence of more active bleeding, however, it is quickly realized that this is but the first step. In most cases immediate tracheotomy at the bedside must be carried out. Following this, the firm packing of the pharynx and mouth with a long, single strip of gauze soaked with albolene or mineral oil lends the greatest assurance for immediate control of the hemorrhage (Fig. 2). Gentle and repeated aspiration of blood from the tracheobronchial tree should next be carried out. The secretions can be kept fluid by the use of small amounts of sodium borate in a 3 per cent solution, dropped directly into the tracheotomy tube, thus lessening the necessity for repeated aspiration of thickened secretions.* Arrangements can then be made, first for supporting the patient by transfusion and parenteral fluids, and next for early ligation of the eroded vessel or its proximal source as soon as the patient's condition permits. The tight gauze packing should be loosened within twenty-four hours, and should be removed from the oropharynx as early as possible in order to prevent extensive pressure necrosis of the pharyngeal wall, which is so prone to occur. Early trial removal is certainly advisable, with repacking of the pharynx only if desperately urgent. The latter measures

are so radical and extreme that they are, of course, reserved for only the most serious hemorrhages defying lesser methods of control. They may overcome the acute emergency, and in an occasional case may be of considerable therapeutic effectiveness.

Deep lacerations and penetrating stab wounds of the head and neck largely arise from such instruments as broken glass, knives, bullets, shell fragments and other piercing metal objects. Wide tangential lacerations usually sever the relatively superficial anterior and lateral jugular veins, and occasionally the deeper-lying inter-

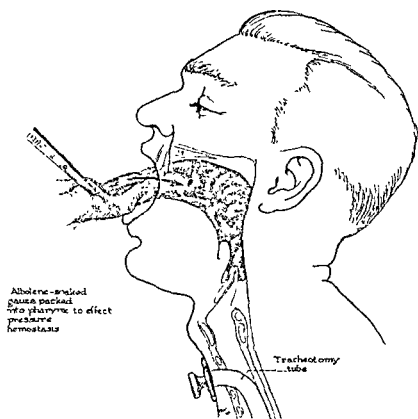


FIGURE 2. *The Second Stage in Attempting to Control Sudden Severe Hemorrhage from the Mouth and Pharynx: Emergency tracheotomy, tight packing of the pharynx with oil-soaked gauze, later ligation of the affected vessel in the neck and early removal of the pharyngeal pack to avoid pressure necrosis.*

nal jugular vein. Penetrating stab wounds more often injure the internal jugular vein, the carotid arteries and the large tributaries of the external carotid artery. In most cases, however, the hemorrhage can be readily and directly controlled by adequate surgical exposure and accurate securing of the bleeding points with hemostat and ligature.

Stab wounds at the level of the base of the skull (second and third cervical vertebrae) may give rise to hemorrhage especially difficult to control. Here the problem may become alarmingly acute and bring into play all available measures, both direct and indirect. Forceful digital pressure above and below the edges of the wound will usually allow time to get the patient to the hospital and to the operating room. Despite generous operative

*This method, employed on the Tracheotomy Service at the Haynes Memorial Hospital, was suggested by Dr. Conrad Westelhof.

enlargement of the stab wound, both the depth of the bleeding area and the massive effusion of blood may frustrate a radical attempt to gain direct exposure of the bleeding vessel or vessels. In addition, the dire possibility of intravenous aspiration of air, leading to air embolus, must be faced. Shock and infection loom as further complicating factors.

Damage to the last four cranial nerves (the ninth, tenth, eleventh and twelfth) and to the cervical sympathetic trunk may occur from a knife or bullet wound through the retroparotid space, producing the serious and characteristic sequelae described by Villaret⁵ as the syndrome of the retroparotid space. Immediately after their exit from the skull, these four cranial nerves lie so close together as to simulate a plexus with the cervical sympathetic trunk. The hypoglossal nerve lies medial to the spinal accessory nerve and winds around the cervical sympathetic, the glossopharyngeal and the vagus nerves, from behind, forward and downward. Hence, injury by

TABLE 1 Possible Results of Nerve Injury in the Retroparotid Space

Results	Nerve Involved
1. Loss of taste on the posterior third of tongue	Glossopharyngeal (ninth cranial) nerve
2. Loss of reflexes of soft wall of pharynx and side of soft palate	
3. Loss of reflexes in pharynx, palate and uvula	
4. Loss of reflexes of soft wall of external auditory meatus	Vagus (tenth cranial) nerve
5. Loss of reflexes of soft wall of external auditory meatus	
6. Loss of reflexes of soft wall of external auditory meatus	Spinal accessory (eleventh cranial) nerve
7. Loss of reflexes of soft wall of external auditory meatus	
8. Loss of reflexes of soft wall of external auditory meatus	Hypoglossal (twelfth cranial) nerve
9. Loss of reflexes of soft wall of external auditory meatus	
10. Loss of reflexes of soft wall of external auditory meatus	Cervical sympathetic nerve trunk
11. Loss of reflexes of soft wall of external auditory meatus	

a stab wound or bullet in this area may involve any or all these nerves—Galen considered the ninth, tenth and eleventh cranial nerves as one, because they are so close together. After the publishing of Villaret's description, additional cases were reported by Pollock⁶ in 1920 and Stookey⁷ in 1922. The clinical findings resulting from such injury are characteristic, and may include some or all the changes listed below. Their recognition may prove helpful in locating the position of a bullet or shell fragment or the exact site of injury from a stab wound. Interestingly enough, the case reported here showed all the changes listed in Table 1.

While Villaret, as stated, regarded the syndrome of the retroparotid space as resulting from injury to the four cranial nerves and the cervical sympathetic trunk, Vernet (cited by Stookey⁷) described

injuries of lesser extent, namely, to the ninth, tenth and eleventh cranial nerves, as the "syndrome of the foramen lacerum."

Injury to the phrenic nerve and to the trachea may further complicate the picture. Control of the hemorrhage remains the primary consideration, however, and this will pave the way for proper management of the accompanying injuries.

CASE REPORT

E. C., a 32 year old shoe worker, was stabbed severely in the upper right posterior side of the neck with a 4 inch long, flat bladed shoe knife, on March 30, 1939. A fellow worker quickly applied manual pressure to stem the rapid flow of blood until the patient's physician, Dr. William A. Flynn, of Amesbury, Massachusetts, arrived five minutes later. At this time blood was pouring freely from the wound and the patient was coughing up blood from the nose and mouth. He was taken by ambulance to the Amesbury Hospital, where Dr. Flynn tightly placed three deep silk sutures through the skin and subcutaneous tissues, in order to close the superficial portions of the wound without drainage. Following this a pressure bandage was applied and parenteral fluids were administered, and the patient did reasonably well, considering the severe loss of blood, until the following morning. While the dressing was being changed he suddenly coughed and blood spurted forcefully from between the sutures. Further serious loss of blood was prevented by having a nurse apply firm digital pressure above and below the edges of the wound until arrangements for operative control could be carried out.

I was asked to see the patient 16 hours after admission to the hospital. Examination revealed a muscular, pale, weakened, conscious man who showed the effects of acute loss of blood. The pulse was 110. The blood pressure was 110/60. Just below the right mastoid process, in the upper right posterior side of the neck, there was an obliquely horizontal, sutured wound 4 cm in length, through the apposed edges of which a large column of blood spurted whenever digital pressure was released. The red cell count was 3,820,000, the hemoglobin 68 per cent (Sahli) and the white cell count 14,950.

A recent attempt to examine the mouth had precipitated further moderate bleeding from the nose and mouth. Later examination confirmed my suspicion that the posterior pharyngeal wall had been pierced just above the level of the soft palate. The uvula and soft palate were grossly discolored, purple and swollen. There was paralysis of the right vocal cord, and a low husky pitch to the voice with thickened speech, difficulty in swallowing and nasal regurgitation. The patient complained of constant accumulation of mucus in the throat.

Immediate operation was carried out under novocain anesthesia. The three widely spaced silk sutures were removed, when a stream of blood 2.5 cm in diameter spouted forth from the extreme depth of the wound, to rise for 10 cm above the level of the skin. This flow was controlled only by having the assistant maintain constant digital pressure along each edge of the wound. The deep clot was removed, the incision generously enlarged and the deep fascial layer firmly retracted with grasping clamps in a radical attempt to gain direct exposure of the bleeding point. Exploration revealed the depth of the wound to be more than 10 cm, the direction obliquely inward and slightly upward toward the pharynx and the

deep tissue injury extensive undoubtedly reaching the pharynx. After a reasonable attempt to control this terrible bleeding which defied exposure the wound was tightly packed with gauze soaked in sterile olive oil.

The patient was then turned on his left side and under novocain infiltration a 5-cm incision was made along the anterior border of the right sternomastoid muscle in the upper third of the neck. The muscle was retracted laterally and the fibers of the underlying sternohyoid muscle were separated longitudinally to expose clearly the bifurcation of the common carotid artery. The external carotid artery was doubly ligated with No. 1 chromic

The patient's course henceforth was good and it was evident that the emergency had passed.

In order to correct the large, gaping wound cavity a secondary closure was carried out on the 8th day after the accident. It is of interest that the patient complained at this time of fairly severe and almost constant right-sided headache lasting since ligation of the external carotid artery and that this persisted with slowly diminishing intensity throughout his 10 days' hospital stay. That the right vagus nerve had been simultaneously injured was evidenced by the paralysis of the right vocal cord (recurrent laryngeal nerve) the low husky voice the difficulty in swallowing and the constant irritation from the pooling of thick mucus and saliva in the throat (superior laryngeal nerve) of which the patient could not rid himself. He was discharged on April 8 the tenth day after the injury with marked improvement in his general condition but with little change in the local disturbances noted above. At that time the red cell count had risen to 4,070,000 and the hemoglobin to 74 per cent.

Two weeks after discharge both wounds were well healed and the patient's general condition was good. He

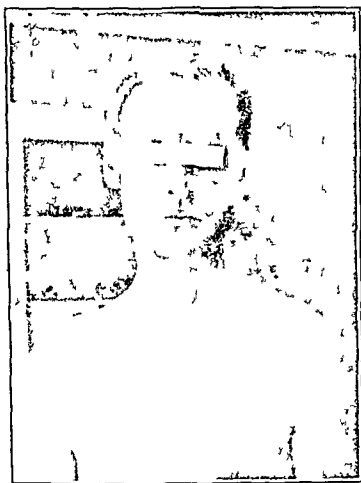


FIGURE 3. Marked Atrophy of the Trapezius Muscle and the Right Neck and Shoulder. (photograph taken eleven months after injury.)

cut out above and below its first branch the superior thyroid artery thereby cutting off the possibility of collateral blood flow from the opposite side of the neck. The wound was closed in layers.

Following this procedure attention was again turned to the stab wound in the neck. The pack was gently removed and for 30 seconds nothing happened. Then blood again poured forth from the depth of the wound in an equally large stream but with less force. It appeared to be coming from the internal jugular vein at the base of the skull with the bleeding from the posterior auricular and occipital arteries probably removed. The wound was tightly repacked with oil soaked gauze a tight pressure bandage was applied and the patient was transfused. Shortly thereafter he was transferred to the Massachusetts Memorial Hospitals, Boston, both for measures of direct control on later removal of the pack and for the facilities of a blood bank if needed.

Forty-eight hours later on April 1 half the pack was removed and in 72 hours the entire pack was removed. Each time the wound immediately filled with slowly welling blood especially on complete removal of the pack. A thin gauze strip covered with vaseline was lightly inserted and the bleeding subsided within the next 5 hours.



FIGURE 4. Hematoxy of the Tongue and Marked Distortion to the Injured Side (photograph taken eleven months after injury.)

still complained of occasional headaches across the entire frontal region.

Seven weeks after the injury, on May 27, the patient stated that he was well except for much trouble with his throat that is it was hard to swallow especially solid foods which threatened to go down the trachea. He had much phlegm daily with marked hoarseness and lowered pitch to the voice. Whereas he had had no headaches before operation he had morning headaches almost every day and occasionally during the day. In addition he called attention to the difference in the size of his eyes. He had a definite right enophthalmos and dilatation of the pupil and complained of marked numbness of the entire right side of the face especially when shaving. Thus a typical Horner's syndrome had resulted from the apparent

severance of the cervical sympathetic chain at the time of the original injury.

Eleven months after the injury, March 6, 1940, the patient halted his heavy outdoor work on the highway to appear for examination. By this time perusal of the literature had drawn my attention to Villaret's syndrome of the retroparotid space. Curiously enough, this patient showed all the evidences of complete extracranial division of the glossopharyngeal, vagus, spinal accessory and hypoglossal nerves, and partial recovery from injury to the cervical sympathetic nerves (Figs. 3 and 4). The syndrome was evident in its entirety.

Signs of Horner's syndrome, though still present, were lessened, in that the enophthalmos and lid narrowing were slight, the pupil was no longer dilated, and the numbness of the right side of the face had disappeared. To

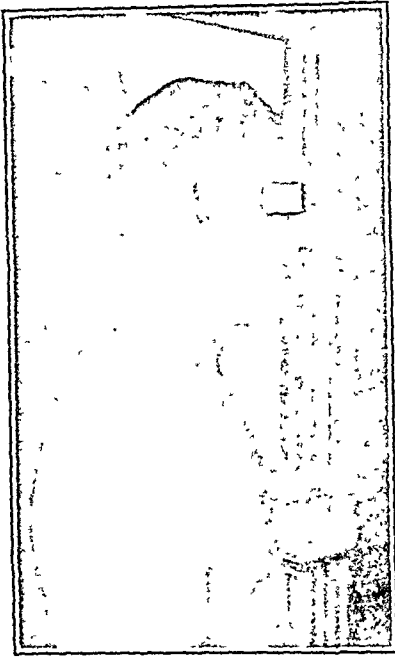


FIGURE 5. End Result.

Both incisions are well healed, and the patient shows a greatly improved nutritional state. This photograph was taken eleven months after injury.

the remaining changes, which had become permanent, the patient had adjusted himself admirably. The voice was low and husky but tired less easily. The right vocal cord was immobile and in the cadaveric position. Mucus in the throat, difficulty in expelling it and dysphagia were still annoying. There was marked atrophy of the right half of the tongue, with sharp deviation to the affected side. There was loss of taste on the right posterior half of the tongue, and numbness of the right external auditory canal. Marked wing deformity of the scapula was present, with atrophy and paralysis of the right trapezius muscle and inability to raise the right arm above the level of the shoulder.

Additionally, the patient stated that 2 months after the injury, or 9 months previously, an abscess had drained for 1 week through the right auditory canal, and that complete deafness of the right ear had resulted. He also complained of steady, throbbing tinnitus of the right side of the head whereby he was conscious of every heartbeat. His headaches had ceased. Both wounds were well healed and the scars not conspicuous (Fig. 5). Despite the disturbances noted the patient was in excellent general

health, enjoying life and being actively engaged in outdoor manual labor.

In this case, ligation of the external carotid artery diminished but did not in any manner control the hemorrhage. The persistent nonarterial bleeding suggested severance of the internal jugular vein at a level close to the base of the skull, just below its emergence from the jugular foramen. At the suggestion of Dr. Alexander S. Begg, of Boston University School of Medicine, evidence of this severance was sought by examining the head of a cross-sectioned cadaver at the level of injury. This allowed clearer visualization of the path of the flat-bladed knife through the deep retroparotid space to the nasopharynx (Fig. 6). It became apparent that the knife blade had

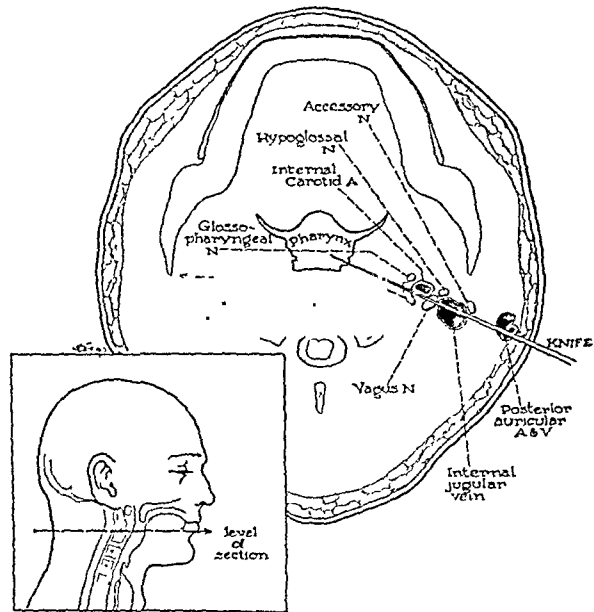


FIGURE 6.

This sketch shows the level of injury (insert) and a cross-section study. The path of the knife blade traverses the retroparotid space. Note the closeness of the uninjured internal carotid artery to the other structures severed, namely, the posterior auricular artery and vein, internal jugular vein, last four cranial nerves, and cervical sympathetic ganglion.

coursed medially, inward and slightly upward, to pass close to the body of the third cervical vertebra, and to sever the posterior auricular artery, the internal jugular vein, the right glossopharyngeal, vagus, spinal accessory and hypoglossal nerves and the cervical sympathetic chain at this high level, and finally to reach and pierce the nasopharynx. Examination of the cross-sectioned head clearly indicated that the knife could not have reached the pharynx along this course without having severed the internal jugular vein. Furthermore, the clinical evidence of injury to the right ninth, tenth, eleventh and twelfth cranial nerves and to the

cervical sympathetic trunk was substantiated by the close anatomic relation of these structures to the internal jugular vein.

Ligation of the external carotid artery without delay, in my opinion, was urgently necessary before placing reliance on gauze packing to control the persistent venous bleeding. It should be mentioned that while the danger of ligating this artery is practically nil if thrombosis extending to the internal carotid artery is avoided by ligating the artery distal to the superior thyroid artery, nevertheless permanent ligation should be done only when absolutely necessary. Neither the condition of the patient nor the circumstances for control of aftercare made temporary occlusion of the artery, by passing an untied ligature around it and strapping it to the skin under traction, dependable or safe.

Ligation distal to the superior thyroid artery is regarded as the site of election, in that it is technically easier, does not endanger the internal carotid artery with thrombosis and cerebral embolism and lessens the collateral blood supply from the opposite side by way of the superior thyroid artery. It must be stated that in the reported case the external carotid artery was ligated both above and below the superior thyroid artery. Fortunately no hazardous sequelae resulted, save for fairly persistent right-sided temporofrontal headache. This gives rise to speculation as to the possibility of avoiding these cerebral symptoms by ligating distally and not proximally to the superior thyroid artery.

SUMMARY

With passing mention of the usual systematic procedures widely employed in the direct control of hemorrhage, emphasis has been more particularly directed toward the management of sudden, severe hemorrhage arising, from the mouth, as in the cancer patient, or from the head and neck following especially deep lacerations of the stab-wound type.

Suggestions for handling such an emergency have been mentioned in detail, with report of a patient manifesting sudden severe hemorrhage from the neck and mouth and extensive injuries to the extracranial nerves. Follow-up examination eleven months after the injury showed all the changes suggested by Villaret in his description of the syndrome of the retroparotid space. The case report is presented as substantiating the accuracy of Villaret's original description of this characteristic post-traumatic nerve-injury syndrome.

The site of election for ligation of the external

carotid artery is emphasized for the purpose of preventing any likelihood of cerebral thrombosis and embolism, and of effectively eliminating collateral blood flow from the opposite side through the superior thyroid artery.

CONCLUSIONS

In the majority of even severe hemorrhages, adequate control may be gained by the use of hemostat, ligature, pressure or packing.

Occasionally added resources may become urgently necessary in order to control hemorrhage from intraoral cancer and deep lacerations of the head and neck, especially of the stab- and bullet-wound types.

Although in many cases massive hemorrhage from the mouth may rapidly become fatal, methods of quick, orderly approach such as immediate intraoral and extraoral manual pressure, tracheotomy, followed by gauze packing of the pharynx, and later proximal ligation of the affected vessel, may help in controlling the emergency and in the eventual salvage of the patient.

Likewise, deep lacerations of the stab- and bullet-wound types may require any or all these measures to control the hemorrhage.

Injury in the region of the retroparotid space is very likely to sever the last four cranial nerves—glossopharyngeal, vagus, spinal accessory and hypoglossal—and the cervical sympathetic trunk. This gives rise to characteristic changes described by Villaret in 1917 as the syndrome of the retroparotid space.

The characteristics of this syndrome are easily recognizable, seriously damaging and usually permanent.

Control of such massive hemorrhage and recognition of these extracranial-nerve injuries have been illustrated in the case reported here. Villaret's syndrome was evident in its entirety, especially at examination eleven months after injury.

Ligation of the external carotid artery should be done only when urgently necessary, for complications do occur. The artery in most cases should be ligated just distally to its first branch, the superior thyroid artery, in order to prevent thrombosis extending to the internal carotid artery, and to eliminate collateral blood flow from the opposite side via the superior thyroid artery.

412 Beacon Street

REFERENCES

1. Stookey, B.: *Surgery of the nerves*. Nelson New Loose-Leaf Surgery. Vol. 2. New York: Thomas Nelson & Sons, 1937. P. 555.
2. Semken, G. H.: *Surgery of the neck*. Nelson New Loose-Leaf Surgery. Vol. 2. New York: Thomas Nelson & Sons, 1937. P. 773.
3. Pollock, L. J.: Extracranial injuries of multiple cranial nerves. *Arch. Neurol. & Psychiat.* 4:517-528, 1920.
4. Stookey, B.: *Surgical and Mechanical Treatment of Peripheral Nerves*. 475 pp. Philadelphia: W. B. Saunders Co., 1922. P. 421.
5. Villaret, M.: Le syndrome de l'espace rétro-parotidien postérieur. *Paris méd.* 23:430, 1917.
6. Villaret, M., and Faure-Beaulieu, M.: Le syndrome nerveux de l'espace rétro-parotidien postérieur. *Presse méd.* 26:591-593, 1918.

THE CLINICAL MANAGEMENT OF BREAST TUMORS*

GRANTLEY W. TAYLOR, M.D.†

BOSTON

THERE are two questions of practical importance in the clinical management of breast tumors: What is the nature of the tumor? What is the appropriate treatment for this type of tumor? It is at once obvious that the answer to the second question cannot be arrived at until the first has been answered completely and accurately. It has seemed worth while to inquire into the accuracy of the clinical diagnosis of breast tumors. A review has therefore been made of the 127 breast tumors subjected to operation at the Pondville Hospital in 1938 and 1939.

Our policy is to recommend prompt exploration in all cases of breast tumor. The patient's permission to carry out whatever surgery may be necessary is secured. The exploration is usually performed under general anesthesia, and it is planned to have a pathologist present at the operation when there is any doubt about the diagnosis. A comparison was made between the preoperative and postoperative diagnoses in our series. There was a clinical error in diagnosis in 28 cases, or 22 per cent. This is a rather high percentage of error, but it does not begin to describe the difficulties in clinical diagnosis. In many cases a presumptive diagnosis which eventually proved to be accurate had been made, but it was necessary to confirm it by immediate pathological examination. It is interesting to find that in 45 cases the tissue was subjected to frozen-section diagnosis, and that in an additional 36 cases immediate gross pathological examination was carried out in order to confirm the diagnosis. Thus, in 56 per cent of the cases pathological help was employed at the time of operation (Table 1).

It may at once be pointed out that many of the operations at the Pondville Hospital are carried out by younger men who have less extensive experience with the clinical aspects of these diseases, and who derive some satisfaction from immediate pathological confirmation of the diagnosis. On this account it may be urged that the number of immediate pathological examinations is excessive. If in the hands of more experienced surgeons it is necessary in fewer cases to have a pathologist present at the time of operation, this means simply that in these cases the surgeon is acting as his

own pathologist in interpreting the gross appearance of the tumor and in basing his decision on this finding. In this sense it may be said that the more experienced surgeons depend on pathological examination just as freely as do the younger men. Furthermore, a resident pathological staff is ready and willing at all times to be present in the operating room to carry out immediate examinations, and perhaps for this reason an excessive number of such examinations are made. In other hospitals and clinics it may be less convenient or feasible to have a trained pathologist present, but that does not mean that the patient's interests are

TABLE 1. *Diagnosis of Breast Tumors.*

FINAL DIAGNOSIS	No. of Cases	ERRORS IN CLINICAL DIAGNOSIS		IMMEDIATE PATHOLOGICAL EXAMINATION	
		NO.	PER CENT	NO.	PER CENT
Carcinoma	68	7	10	29	43
Chronic cystic mastitis	25	10	40	15	60
Adenofibroma	17	1	6	12	70
Papilloma	7	5	71	5	71
Miscellaneous	10	5	50	10	100
Totals	127	28		71	
General averages			22		56
Frozen-section diagnoses				45	
Errors in frozen-section diagnoses				5	

being well served by the omission of such an examination. In 5 cases in our group of 45 frozen-section examinations the final pathological slide did not confirm the first diagnoses, so that even taking all possible precautions against errors, there is still a chance of inaccurate diagnosis.

In endeavoring to answer the second question—What is the appropriate treatment for this type of tumor?—it may be desirable to ask an additional question in regard to malignant cases; namely, What is the extent of the disease? Taylor and Bruce¹ have pointed out elsewhere that actual clinical appraisal of the extent of the disease is subject to considerable inaccuracy. In the study of axillary examinations in cases of breast cancer we found an error of clinical appraisal in 28 per cent of the examinations. It is probable that error as regards the extension to inaccessible parts of the body are even greater than this figure, in spite of careful x-ray examinations to detect remote metastases. It is sufficient to say that every care must be taken to make sure that the patient is in an operable stage before treatment is begun

*Read at the annual meeting of the Massachusetts Medical Society, Boston, May 21, 1941.

†Instructor in surgery, Harvard Medical School; visiting surgeon, Pondville Hospital, Wrentham, Massachusetts.

When a patient is found to be in this stage and the diagnosis of cancer has been established, if necessary by immediate pathological examination, the treatment of choice is immediate radical breast amputation. This involves removal of the entire breast with its overlying skin, both pectoral muscles, and the axillary lymph nodes and fat as high as the clavicle. No alternative method of treatment can be shown to yield as consistently favorable results as can be secured by radical surgery.

The adenofibromas comprise a very interesting group of tumors which are benign in their behavior. There are no outstanding clinical characteristics aside from the presence of tumor that can be positively depended on. There were 17 cases, and frozen-section diagnosis was employed in over half of them. It is significant that an erroneous clinical diagnosis of adenofibroma was made in an additional 8 cases, 2 of which proved to be cancer. Excision of the tumor alone seems to be all that is necessary in cases of adenofibroma.

There were 25 operated cases in which chronic cystic mastitis was found. A correct clinical diagnosis was made preoperatively in only 15 of these. An erroneous clinical diagnosis of cystic mastitis was made in 7 cases, 3 of which proved to be carcinoma. Immediate pathological examination was employed in 15 of the cases that proved to be chronic cystic mastitis. The proper method of treatment for this condition has not been fully established. In our group, partial resection of the breast was carried out in 12 cases and mastectomy in 13. It has recently been pointed out that chronic cystic mastitis actually constitutes a precancerous condition, in that the breast that is the seat of the disease is more likely to develop cancer subsequently than is a normal breast.² However, this likelihood does not seem to be great enough to warrant advocating a bilateral simple mastectomy in all cases. In our series, operation was carried out in most cases in order to rule out the possibility of cancer.

Intraductal papilloma was found at operation in 7 cases, but a correct clinical diagnosis was made preoperatively in only 2 of these. Immediate pathological examination was carried out in 5 cases, and in 2 of these the frozen-section diagnosis suggested carcinoma so strongly that radical mastectomy was performed. In the remaining cases, excision of the tumor was carried out in 2 and simple mastectomy in 3. This condition also can rea-

sonably be considered to be precancerous, and it is not uncommon to find multiple intraductal papillomas in these patients. Proper surgical procedure in this group also is not fully established. In these cases, as in those of chronic cystic mastitis, it is undoubtedly important to carry out protracted observation because of the possible later development of cancer.

There were 2 patients suffering from sarcoma of the breast, and in 1 of these the clinical diagnosis had not indicated malignancy. Both cases were treated by simple mastectomy. It is probably unnecessary to carry out a radical mastectomy in cases of sarcoma, although it is desirable to remove the fascia overlying the pectoralis muscle, or perhaps even to remove the muscle itself. The disease is slow to metastasize, and most failures in treatment are due to local recurrences. Thus it would seem desirable to be more radical in the treatment of the disease, especially in regard to the extent of dermal and fascial removal.

In 8 cases the final diagnosis proved to involve other conditions such as inflammation, localized area of hypertrophy and fat necrosis. Immediate pathological examination was carried out in all these cases, and all were subjected to operation on the ground that cancer could not be ruled out on clinical evidence.

CONCLUSIONS

It is evident that no breast tumor can be absolutely declared to be noncancerous on the basis of clinical examination alone. Its presence is presumptive evidence of cancer until pathological study has demonstrated the contrary. This means that every breast tumor should be subjected to exploration. The decision as to the proper method of treatment can be based only on accurate knowledge of the nature of the disease.

Benign conditions that are encountered at exploration are probably adequately treated by removal for examination. Malignant tumors should be subjected to radical surgery without undue delay. It is only by the following of these principles that any considerable improvement in the management of tumors of the breast can be expected.

264 Beacon Street

REFERENCES

1. Taylor, G. W., and Bruce, N. H. Prognostic factors in carcinoma of the breast. *New Eng. J. Med.* 222: 90-92, 1940.
2. Warren, S. Relation of chronic cystic mastitis to cancer of the breast. *Surg. Gynec. & Obst.* (in press).

ROCKY MOUNTAIN SPOTTED FEVER*

An Analysis of Seven Cases, Including One Laboratory Infection

EUGENE P. CAMPBELL, M.D.,† AND WALTER H. KETCHUM, M.D.‡

PHILADELPHIA, AND WASHINGTON, D. C.

RECENT investigations of the rickettsial diseases by Zinsser,¹ Dyer,² Lillie,³ Topping⁴ and others have added materially to our knowledge of this group of infections. Rocky Mountain spotted fever, first described by a United States Army surgeon⁵ in 1896, was found by Wilson and

varieties, there is little if any clinical basis for differentiating them.

From 1931 to 1939, 7 patients with Rocky Mountain spotted fever were treated at the Walter Reed General Hospital in Washington. Three of them died. One patient, a physician, contracted the Western type of infection while working with the virus in the laboratory. A report of this case follows.

N. T., a 31-year-old physician, was admitted to the Walter Reed General Hospital on December 30, 1938, because of his own diagnosis of Rocky Mountain spotted fever.

The past and family histories were not important except that 2 months before onset the patient had received part of a course of Parker-Spencer vaccine, which caused his Weil-Felix reaction to be positive in a titer of 1:80. During the course of certain experimental studies on virulent Western tick virus he accidentally became infected, 11 days before admission and 6 days before the first symptoms of general malaise and headache. During the 5 days preceding hospitalization the patient noted pain in the eye muscles and joints, weakness, chills, fever and finally a rash on the hands.

Physical examination revealed a dejected man with a "hangover" appearance. There was a sparse petechial rash on the back of the hands. The pharynx was injected. The temperature was 103.8°F., the pulse 111, and the respirations 24. Otherwise the examination was normal.

The essential laboratory findings are summarized in Table 1 (Case 1). The Weil-Felix reaction, which was positive in a titer of 1:80 on admission, became negative following the infection and remained so for 1 year. Roentgenograms, electrocardiograms, blood cultures and other laboratory studies were normal. The Western type of virus was recovered from a guinea pig injected with the patient's blood on the 4th day after onset.

The febrile period lasted 19 days, the fastigium occurring on the 13th day with a temperature of 105°F. The temperature varied between 100 and 105°F., with the lowest levels occurring during the morning hours. The pulse varied from 90 to 140, and in general varied directly with the temperature. The rash spread to involve the whole body (Fig. 2), including the palms of the hands, the soles of the feet and even the optic fundi. It began to fade on the 20th day, giving place to a fine, powdery desquamation. Throughout the course of the disease the patient complained of severe photophobia, diplopia, soreness of the throat and pains in the muscles and joints. Marked mental cloudiness and irritability were the only neurologic features noted. He eventually made a complete recovery.

A study of the seasonal prevalence of Rocky Mountain spotted fever by Hampton and Eubank⁸ shows that the season of high incidence for the Eastern variety begins in May, reaches a peak in

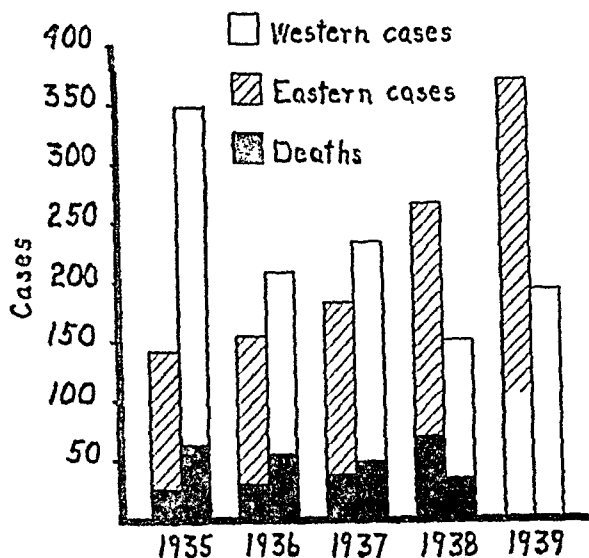


FIGURE 1. Case and Death Incidences of Rocky Mountain Spotted Fever in the United States (1935-1939).

The western cases include those from Montana, Idaho, Wyoming, Colorado, New Mexico, Arizona, Utah, Nevada, Washington, Oregon and California; the eastern cases, those from all the other states. No cases were reported from Maine, New Hampshire, Vermont, Connecticut and Wisconsin.

Chowning⁶ in 1904 to be transmitted by a tick. The etiologic agent was identified by Ricketts⁷ in 1909. It is a truly American disease.

Much interest has been aroused by the increasing incidence of Rocky Mountain spotted fever in the eastern United States (Fig. 1). Only five of the forty-eight states have yet to report this disease, and although the incidence is not great, enough deaths have occurred to make it a serious medical problem. Aside from an academic interest in the relation between the Eastern and Western

*From the Walter Reed General Hospital, Washington, D. C.

†Assistant professor of epidemiology, Department of Public Health and Preventive Medicine, University of Pennsylvania, Philadelphia; assistant physician, Philadelphia General Hospital.

‡First Lieutenant, Medical Reserve Corps, United States Army

ily and declines in August and September. Of 16 cases of the Eastern type, 1 occurred in May, in June, 2 in July, 1 in August and 1 in November. Five cases were related to the bite of a tick. The sixth was an accidental laboratory infection with the Western tick virus. The seventh was contracted from an unknown source.

In 4 cases the period of time from the tick bite to the introduction of the virus to the onset of symptoms was given as five days in 1 case, six in 2 and seven in 2. In the fifth patient, a dog fancier, the incubation period could not be determined because he had been picking ticks from his dogs

lieve that the characteristics serving to differentiate these cases were in no way sufficient in themselves to be of general differential value. The incidence of the various signs and symptoms occurring in the 7 cases is given in Table 2.

Case fatality studies of 2036 cases were made by Hampton and Eubank⁸ in 1937. They found that during the period from 1933 to 1937, 1435 cases of the Western type had a fatality rate of 19.4 per cent. During the same period 601 cases of the Eastern type had a fatality rate of 18.1 per cent. There was thus little difference in the fatality in the two varieties. Our 6 cases of the Eastern type

TABLE 1. *Essential Laboratory Data* in 7 Cases of Rocky Mountain Spotted Fever.*

CASE NO	AGE	SEX	WHITE CELL COUNT × 10 ⁹	WEIL-FELIX REACTION	REMARKS
1	31	M	12 0-22 0	Positive 1 80 (<i>Proteus</i> OX 2 19)	Recovered, guinea pig inoculated on 4th day of illness positive for Western type of virus
2	41	M	12 5-14 5	Positive 1 40 (<i>Proteus</i> OX 19c)	Died, necropsy
3	42	M	6 0-19 0	Positive 1 1280 (<i>Proteus</i> X)	Recovered
4	39	M	9 0-18 0	Positive 1 160 (<i>Proteus</i> OX 2 19)	Recovered
5	21	M	6 0-21 0	Negative	Died necropsy
6	28	M	7 0-11 0	Positive, 1 640 (<i>Proteus</i> OX 19c)	Recovered
7	7	M	5 0-16 0	Positive 1 5120 (<i>Proteus</i> OX 19)	Died necropsy †

*Albumin, casts and cells were commonly found in the urine from all cases during the febrile period

†Necropsy findings previously reported¹⁵

for several days. The sixth patient contracted the infection while hunting rabbits, seven days before his first symptoms. The seventh patient had taken several horseback rides into the mountains near Front Royal, Virginia, and had removed ticks from his body on many occasions. The appearance of the rash in 5 cases followed the onset of symptoms in one, two, three, three and five days, respectively.

It is unusual for a case of the Western type and one of the Eastern type to be treated in the same hospital at the same time. The courses of Cases 1 and 3 given in Table 1 overlapped, offering an opportunity to compare the clinical features of the two varieties. In Case 1, reported above, the physician-patient made many interesting and accurate observations of the symptoms and course of events. In comparison with the Eastern type of disease in Case 3, the Western type of infection was more severe: there was a more intense and widely distributed rash; the febrile period was longer, and the average elevation of the fever was well above that of Case 3. The headache, muscle pains and arthritic symptoms were more severe. Small petechial retinal hemorrhages were noted, but were not found in 2 of the patients infected with the Eastern type of virus. The prophylactic injection of the vaccine in Case 1 may have altered the features of the disease to some extent, but we be-

lieve that the characteristics serving to differentiate these cases were in no way sufficient in themselves to be of general differential value. The incidence of the various signs and symptoms occurring in the 7 cases is given in Table 2.

Case fatality studies of 2036 cases were made by Hampton and Eubank⁸ in 1937. They found that during the period from 1933 to 1937, 1435 cases of the Western type had a fatality rate of 19.4 per cent. During the same period 601 cases of the Eastern type had a fatality rate of 18.1 per cent. There was thus little difference in the fatality in the two varieties. Our 6 cases of the Eastern type

TABLE 2. *Signs and Symptoms Occurring in 7 Cases of Rocky Mountain Spotted Fever*

SIGN OR SYMPTOM	NO OF CASES	SIGN OR SYMPTOM	NO OF CASES
Rash	7	Desquamation	2
Fever	7	Photophobia	2
Mental disorientation and irritability	6	Nausea	2
Headache	5	Weakness	2
Chills	5	Convulsions	1
Chemosis and injection of conjunctivae	5	Diarrhea	1
Generalized aches and pains	4	Jaundice	1
Meningeal irritation	3	Vomiting	1
Palpable spleen	3	Pains in muscles	1
Pneumonia	3	Sweating	1
Coated tongue	3	Anorexia	1
		Cough	1
		Hiccough	1
		Diplopia	1

cases with an unexplained fever associated with a rash. Despite this fact, it seems probable that many cases of mild infection are passed over too lightly by the busy physician and go unrecognized. It is important to encourage careful habits of thinking on the part of physicians in order that the chief characteristics of the case in question shall bring to mind a number of diagnostic possibilities.

The situation in which the patient is acutely and seriously ill with the cardinal symptoms noted above deserves prompt and thorough study. Time is often a chief consideration in the patient's chances for recovery. Once the proper diagnostic

type of reaction has not been observed in guinea pigs inoculated with the Eastern strains of the virus. The test was performed in 3 of our 7 cases; a positive result was secured in 1 (Case 1). Scrotal edema and necrosis in human beings was noted



FIGURE 2. Fully Developed Rash in a Case of Western Type of Rocky Mountain Spotted Fever (United States Army Medical Museum, Negative No. 67987).

suggestion has been made, the progress of the case, in addition to the results of diagnostic procedures, seldom leads one away from the correct diagnosis.

The Weil-Felix reaction usually becomes positive between the eleventh and nineteenth days.⁹ To ensure the best results three tests should be made: one as soon as possible after the onset, the second after ten days and the third during convalescence. The rise and fall of the agglutination titer is of great diagnostic importance. A titer of 1:160 in a case in which the first Weil-Felix reaction was negative is diagnostic. In some cases the titer may go as high as 1:5120. Depression of a vaccine-produced titer of 1:80 occurred in Case 1. Even after a year, no agglutinins for the various OX strains of the proteus bacillus had appeared in the blood. A satisfactory explanation for this curious though not unique phenomenon has not been advanced. By analogy it seems reasonable to suppose that the degree of immunity cannot be measured by the degree of agglutination titer.

In the Western type of infection in guinea pigs a scrotal reaction, consisting of edema, redness and occasionally necrosis, results from the rickettsial invasion of the skin and subcutaneous tissues. This

by Wood⁷ in his series of collected reports published in 1896.

The significant necropsy findings in our 3 fatal cases were generalized petechial and hemorrhagic skin eruptions. Subserous hemorrhages were found in the heart, brain, kidneys, bladder and lungs. Areas of focal necrosis were noted in the heart, brain, spleen, kidneys and testes in Case 2. Acute splenic tumors—200 gm. in Case 2, 380 gm. in Case 5—of the septic type with sinusoidal engorgement were found in 2 cases. The third (Case 7) showed a spleen weighing 150 gm. with hemorrhagic foci and small pools of blood involving the Malpighian corpuscles. Bronchopneumonia was present in all 3 cases. Cortical hemorrhages occurred in the right adrenal gland in Case 5. Perivascular and petechial hemorrhages were found throughout the white matter of the brain in all cases.

Treatment consists of general measures to maintain the patient throughout the febrile period, such as the administration of intravenous fluids, sedatives, and digitalis if signs of myocardial failure or arrhythmia appear. There is no specific treatment. Vaccines, useful in prevention, are of no value. Sulfanilamide was tried in Case 3, without benefit. Others^{10,11} have reported un-

vorably on the use of both sulfanilamide and ifapyridine. The production of a potent antium has been attempted by Ricketts and Gomez,¹⁸ Heinemann and Moore¹⁹ and by Noguchi.²⁰ No record was made by any of these authors of the use of antiserum in human cases. Topping²¹ reports the beneficial effects of immune serum in the treatment of this disease in guinea pigs and monkeys. It is hoped that his studies will lead to the development of a specific therapeutic agent which to treat this highly fatal malarial man.

SUMMARY

The clinical and laboratory features of 6 cases of the Eastern type of Rocky Mountain spotted fever, with necropsy findings in 3 cases, are reported.

One case of the Western type, an accidental laboratory infection, is described in detail.

REFERENCES

- 1 *Virus and Rickettsial Diseases With especial consideration of their public health significance. A symposium held at the Harvard School of Public Health June 17-June 17, 1931.* 907 pp. Cambridge: Harvard University Press, 1940.

- 2 Dyer R F. The rickettsioses of North America. *Tr College Phys Philadelphia* 7:232-259, 1939.
- 3 Lillie R D, Dyer R E and Topping N H. Cerebral pathology in rodents in endemic typhus and Rocky Mountain spotted fevers. *Pub Health Rep* 54:2137-2148, 1939.
- 4 Topping N H. Rocky Mountain spotted fever: treatment of infected laboratory animals with immune rabbit serum. *Pub Health Rep* 55:41-46, 1940.
- 5 Spotted fever as reported from Idaho. *Report of Surgeon General of United States Army* 1896. Pp 60-65.
- 6 Wilson L B and Chowning W M. Studies in pyroplasmosis hominis (spotted fever or tick fever of the Rocky Mountains). *J Infect Dis* 1:39-57, 1904.
- 7 Ricketts H T. A micro-organism which apparently has a specific relationship to Rocky Mountain spotted fever: a preliminary report. *J M* 4:52-57, 1909.
- 8 Hampton B C and Fulank H G. Rocky Mountain spotted fever: geographical and seasonal prevalence, case fatality, and preventive measures. *Pub Health Rep* 53:584-990, 1938.
- 9 Davis G I, Parker R R and Walker M E. Further observations on the agglutination of protease A strains in Rocky Mountain spotted fever. *Trs Health Rep* 49:298-311, 1934.
- 10 Topping N H. Experimental Rocky Mountain spotted fever and endemic typhus treated with protosol or sulfa pyridine. *Pub Health Rep* 54:1143-1147, 1939.
- 11 Welch N A and Jakubov P J. Rocky Mountain spotted fever: a case report. *Neu Eng J Med* 221:937-939, 1939.
- 12 Ricketts H T and Gomez L. Studies on immunity in Rocky Mountain spotted fever. *J Infect Dis* 5:221-244, 1908.
- 13 Heinemann P G and Moore J J. Experimental therapy of Rocky Mountain spotted fever. *J Infect Dis* 10:294-304, 1912.
- 14 Noguchi H. Immunity studies of Rocky Mountain spotted fever: usefulness of immune serum in suppressing an impending infection. *J Exper Med* 37:383-394, 1923. Immunity studies of Rocky Mountain spotted fever: prophylactic inoculation in animals. *Ibid* 38:605-607, 1923.
- 15 Lillie R D. Pathology of the Eastern type of Rocky Mountain spotted fever. *Pub Health Rep* 46:7840-2851, 1931.

REPORT ON MEDICAL PROGRESS

UROLOGICAL SURGERY: THE URETHRAL CATHETER*

WILLIAM C. QUINBY, MD†

BOSTON

DURING the last few years, especially since extensive employment of the transurethral resection of the prostate came into vogue, the whole problem of catheter drainage of the bladder has been receiving increased attention. This is due to the initiation or increase of infection of the urethra and bladder, which has been considered an inevitable complicating factor following the use of the inlying catheter. Such infection, even though mild, is always undesirable, but in cases in which the prostate has been removed either by the suprapubic or, better, by the perineal route, the outlet of the bladder is likely to be more thoroughly freed of all obstructing tissue than when the transurethral approach is used. Following complete freeing of the bladder outlet, the cystitis that remains after healing has taken place is usually of moderate severity only, and responds quickly to lavage of the bladder with antiseptics. Or it may occasionally be overcome spontaneously after a few weeks. On the other hand infection of the

bladder following a transurethral prostatectomy not infrequently increases in severity, so that in some cases the patient is found to have exchanged his symptoms of obstruction for the more disagreeable and uncomfortable ones of frequent and painful urination. And if there still remains a residual urine, only with great difficulty can the bladder be made sterile again by postoperative lavage or by drugs.

That this is not a necessary sequel of transurethral prostatectomy is evidenced by the experience of Thompson and Buchtel,¹ who find that after sufficient hyperplastic prostatic tissue has been thus removed, patients tolerate the postoperative inlying catheter well without evidence of increasing urethritis and cystitis. Others have been less fortunate, however, so that one often finds the expected benefits vitiated by persisting infection.

Because of infection, therefore, we find a general tendency today to subject patients to catheter drainage of the bladder before operation less frequently and for a much shorter time than formerly. In point of fact, in 96 out of 200 cases

*From the Urological Clinic, Peter Bent Brigham Hospital, Boston.
†Clinical professor of urology, Harvard Medical School, and lecturer, Peter Bent Brigham Hospital.

analyzed by Thompson and Buchtel no preliminary drainage was instituted, even though the blood urea nitrogen at the time of operation was 50 mg. per 100 cc. in 16 per cent of the patients. That so large a proportion of patients could undergo successful removal of the prostate by whatever method without preliminary drainage of the bladder reflects the fact that patients today are being referred for operation at an earlier stage of their difficulties, when the renal function is still intact or only slightly impaired. This is as it should be. The experience of these authorities also points to the fact that drainage of the bladder after operation, if there be no complicating infection, is often sufficient to relieve the embarrassment of the kidneys quite as efficiently at this time as when catheter drainage is employed as a preoperative step.

But in spite of newer knowledge and experience as to when the use of the catheter may be avoided, it is nonetheless an invaluable instrument demanding frequent use. Further studies have been made by Schulte² as concerns the bacteria to be found in the normal urethra of man. Of the four groups of patients chosen for study, none had had any previous infection of the urinary tract and none had any symptoms referable to it at the time of examination. In the first group, after cleansing of the glans with alcohol the second portion of the voided urine was examined bacteriologically. The organisms found in order of frequency were: micrococcus, diphtheroids, *Streptococcus faecalis*, alpha streptococcus, gamma streptococcus, *Staphylococcus albus*, *Escherichia coli*, *Aerobacter aerogenes* and pseudomonas. From a second group the urine was collected by catheter, with the same result except that the number of colonies was somewhat smaller. In the third group the second portion of the voided urine was cultured after the urethra had been gently irrigated with a solution of potassium permanganate. Half these cases still showed the micrococcus. In this group the prostatic secretion was studied as well, and was found in practically all cases to contain an alpha streptococcus. Schulte concludes, therefore, that the micrococcus is a normal inhabitant of the anterior urethra, while the alpha streptococcus is normal for the posterior urethra and prostate. A fourth group of patients, consisting of an approximately equal number of men and women, were studied at cystoscopy. Here also organisms were present, so that Schulte concludes that the urine from the bladder contained urethral bacteria, and that it is impossible to pass a cystoscope into the bladder through the urethra without contaminating the urine. While most clinical urologists will disagree with this last statement, basing their opinion on

the many sterile cultures of the urine obtained in the routine examinations of the clinic, nevertheless the extreme prevalence of bacterial organisms in the male urethra is again emphasized by this study.

Granting the above, and in view of the fact that the use of the catheter is frequently imperative, the problem becomes one of ways and means to prevent increase of infection during such time as its employment is necessary. Basing his conclusions on the undoubted fact that trauma to the urethral walls caused by the catheter plays a large role in promoting growth of bacteria already present, Middleton³ presents an argument favoring abolition of the retention (inlying) catheter in the preparation of all patients for prostatic surgery. He compares the transurethral enucleation of the prostate through a highly inflamed, edematous urethra to removing a cataract in the presence of acute conjunctivitis. Therefore, to avoid this urethritis he advocates intermittent or interval catheterization in the preoperative preparation of all patients. A male nurse or specially trained orderly is instructed to empty the patient's bladder by catheter at three- or four-hour intervals. A soft-rubber catheter (No. 16 Fr.) bearing a coude olive-tip is inserted by the use of a sterile clamp and is not touched by the operator's hand. The objection that relief of embarrassed renal function may not be so prompt and definite by this interval catheterization as when the bladder is kept continuously empty by the inlying instrument, Middleton answers by noting that in normal life the bladder is emptied only intermittently. The rare case in which the catheter cannot be passed without a stilet, or in which bleeding follows its use, he still treats by continuous drainage.

In reply to Middleton's advocacy of the intermittent type of catheterization, Vose⁴ stresses the value of the continuous catheter, when strict attention is paid to surgical cleanliness, to the use of a small, non-irritating size of catheter and to the elimination of occlusive strapping at the meatus. He maintains sterility by an entirely closed system of tubing, and a closed irrigation system when this is needed. He believes that the small catheter (No. 12 to No. 16 Fr.) allows opportunity around itself for drainage of any urethral products of inflammation at the meatus by not overdistending the urethra. Cumbersome adhesive-plaster holding devices have been eliminated by the use of a self-retaining catheter of the Foley type.

Recognizing the various drawbacks to both intermittent and continuous catheterization, and basing our argument on the fact that for the best and most consistent surgical end results, elimination of infection of whatever degree is imperative, we adopted at the clinic of the Peter Bent Brig-

ham Hospital about two years ago still another method of using the catheter for the preoperative treatment of patients with prostatic retention. This method consists in introducing the catheter into the bladder just above the symphysis by the aid of a trocar and cannula. Thus the urethra is spared, while the more extensive suprapubic wound of the former two-stage prostatectomy is avoided. That the method endangers the peritoneum is true only when employed by the grossly inexpert. In point of fact the procedure is one at which the average house officer becomes quickly adept, familiar as he performs it today with the frequent use of varieties of needles and trocars for parenteral medication. In the report of our experience with this method of bladder drainage by Austen⁵ there is cited no case of injury to the peritoneum, and only two in which feared leakage of urine into the prevesical space made subsequent open suprapubic cystostomy advisable. The details of the introduction of the catheter are given by Austen as follows: The bladder must be tensely filled so as to be easily palpable above the symphysis pubis. If this is not already the case a urethral catheter should be introduced and the bladder filled to capacity. After shaving and sterilization of the operative field an area of local anesthesia is produced in the midline. In this area a small vertical incision 0.5 to 1 cm. in length is made through the skin and fascia just above the symphysis. The long needle of the apparatus devised by Kreutzmann⁶ is plunged inward and downward behind the symphysis. When the bladder is entered, urine immediately trickles out through the needle. Should this not occur, the needle must be reinserted. The trocar and cannula are then passed over the needle, and by a slight rotary pressure the entire instrument enters the bladder guided by the needle. The needle and trocar are next removed and a No. 18 Fr. graduated catheter of soft rubber is introduced through the cannula. The cannula is then withdrawn, leaving the catheter in place for drainage. A single silk suture through catheter and skin fixes it at a level of about 12 cm. from the surface, and the outer end of the catheter is connected to a sterile drainage system.

In an editorial Creevy⁷ discusses the care of the postoperative retention of urine. Three factors are held responsible for this retention: the dorsal position of the patient, the painful musculature of the abdominal wall and drugs. Creevy finds a definite tendency of opiates to increase the tonus of the internal vesical sphincter, and also to make the patient unaware of the fullness of his bladder until it is overdistended. Some surgeons withhold

catheterization until prolonged painful distention of the bladder has rendered the situation intolerable. Such distention causes mucosal and submucosal hemorrhages, together with loss of tone to the detrusor muscle and subsequent vesical infection.⁸ Note should always be made of the patient's fluid intake. It is entirely illogical to order a liter of fluid to be given intravenously just after operation, and at the same time to insist that catheterization, if necessary, be postponed at least eight hours. If retention persists so that more than three or four catheterizations are needed, Creevy advises that the instrument be made indwelling and connected to one arm of a sterile glass Y tube by rubber tubing, attached to a sterile reservoir hung at the bedside and containing sterile or antiseptic fluid. The other arm of the Y tube goes to a covered sterile empty bottle beneath the bed. This avoids the contamination inevitable when the bladder is irrigated by hand. The indwelling catheter should not be removed until the patient has gained strength enough to move about in bed. After its removal, the bladder should be tested several times for residual urine. In cases showing loss of bladder function due to lesions of the nervous system, Creevy first empties the bladder by the Credé method at more or less frequent intervals. If this is not possible, he institutes tidal drainage after the method of Munro.⁹

A series of 84 general surgical cases in which urinary retention occurred after operation has been studied bacteriologically by Stalker and Schulte.¹⁰ None of the patients had had previous urinary infection. In the first group of 73 patients the catheter was used intermittently to relieve the retention. The second group consisted of 11 patients put on constant urethral drainage at the time of operative resection of the rectum for cancer. As a result of this study the authors find that patients with postoperative urinary retention following general surgical procedures are best treated by frequent intermittent catheterization, if possible. This can usually be carried out for a period of two to four or more days without the development of evidence of urinary-tract infection. When the indwelling catheter has been used, infection invariably develops in twenty-four to thirty-six hours. Once bacteria have developed, they increase rapidly in number while the catheter is retained. When intermittent catheterization is employed, the increase is not so rapid, and in some cases even a decrease is noted. In many cases in which only a few bacteria are present in the urine, the patients have no clinical symptoms of infection of the urinary tract. Frequently these bacteria gradually disappear without treatment, and for this reason the presence of a

positive culture alone is not sufficient to warrant instituting therapy. However, when the number of bacteria increases rapidly, and especially when this increase occurs where residual urine is present, clinical symptoms of infection are almost certain to occur, and therapy is required. In the group of patients maintained on indwelling catheters, prophylactic treatment was instituted by the use of sulfanilamide, 1 gm. daily, from the time of operation until voluntary urination was resumed. The resulting concentration of sulfanilamide in the urine—35 mg. per 100 cc.—was sufficient to render the urine bacteriostatic. The writers believe that in their experience such prophylactic use of sulfanilamide has been definitely beneficial, for while it does not suffice to keep the urine free of bacteria in every case, it keeps down the number of bacteria and prevents the development of clinical symptoms.

Our present attitude toward the catheter and its use can therefore be summed up somewhat as follows:

It is an indispensable instrument, but its use should always be attended by extreme aseptic precautions.

The urethra, in both men and women, normally harbors bacteria of various sorts which cannot be eradicated permanently.

The inevitable trauma, though slight, following the passage of a catheter through the urethra, or especially that following its permanent use, permits increased growth of these bacteria, with resultant urinary infection—always of the bladder, sometimes of one or the other kidney.

The use of the indwelling catheter should be accompanied by the creation of a bacteriostatic urine through the administration of sulfanilamide, as well as by daily or twice daily irrigation of the bladder with an actively antiseptic solution.

An increasing recognition of the dangers attending the use of the catheter in the urethra is evident. This recognition has taken the form on the one hand of a definite increase in the number of patients who are subjected to prostaticotomy without preliminary drainage of the bladder, and on the other hand, when the catheter must be used, of the introduction of it by the method of suprapubic puncture, thus avoiding the urethra.

Renewed emphasis is found of the importance of careful postoperative attention to the bladder in order to prevent its overdistention.

REFERENCES

1. Thompson, G. J. and Buchtel, H. A. Transurethral resection of large prostate: review of two hundred cases in which 25 grams or more of tissue was removed. *J. Urol.* 36:43-56, 1936.
2. Schulte, T. L. Newer methods in a study of the bacteriology of urinary tract: preliminary report. *Proc. Staff Meet., Mayo Clin.* 14:249-254, 1939.
3. Middleton, R. P. A plex for the abolition of the retention catheter in the preparation of patients for prostatic surgery. *J. A. M. A.* 114:2368, 1940.
4. Vose, S. N. Abolition of the retention catheter. *J. A. M. A.* 115, 1940.
5. Austen, G., Jr. Suprapubic trocar drainage of the bladder. *Ann. Surg.* (in press).
6. Kreuzmann, H. A. R. An improved suprapubic trocar and cannula. *J. Urol.* 40:341, 1938.
7. Creevy, C. D. Care of the urinary bladder after operation. *Surg. Gynecol.* 7:423-426, 1940.
8. Idem. Distention of the urinary bladder. *Arch. Surg.* 28:948, 1934.
9. Munro, D., and Hahn, J. Tidal drainage of the urinary bladder. *New Eng. J. Med.* 212:229-239, 1935.
10. Stalker, L. K., and Schulte, T. L. A bacteriologic study of postoperative retention of urine. *Proc. Staff Meet., Mayo Clin.* 14:730-734, 1939.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTENMORTEM AND POSTMORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C CABOT

TRACY B MALLORY, M.D., *Editor*

CASE 26401

PRESENTATION OF CASE

A forty-two year-old man was admitted to the hospital complaining of attacks of postprandial precordial pain, and dyspnea on exertion.

Eight weeks before admission the patient developed what he called "indigestion pains" following meals, located high under the left lower ribs. These non radiating pains occurred in attacks, lasting a few minutes, and were usually the result of hurried eating and also produced by physical exertion. Following one of these attacks, he developed dyspnea, which forced him to sit down. During the eight week interval before admission, he fainted two or three times; each time there were no prodromal symptoms, and he remained unconscious for from two to five minutes. Six weeks before entry orthopnea appeared, which on a few occasions forced him to sit upright in a chair throughout most of the time. Three and again two weeks before admission he developed ankle edema, and a fear of the ingestion of food because of the vomiting it engendered. One week before entry he was seen by a physician, who prescribed a pill of digitalis three times a day; he had taken a total of 15 pills at the time of entry.

About one year before entry the patient badly injured the left fourth and fifth fingers. An attempt was made to save one finger, two surgical operations were performed on it, but they were unsuccessful. It was stated that during this time the patient suffered pains that he often described as radiating up the arm to his "heart." He had had pneumonia twice nineteen years before admission. Tonsillectomy and adenoidectomy had been performed fourteen years before admission. He gave no history of rheumatic fever or scarlet fever. The family history was negative.

Physical examination revealed an orthopneic, acutely ill, cold and clumsy man whose neck veins were markedly distended and who displayed Cheyne Stokes respirations. The pupils were equal but reacted sluggishly to light. The tongue was red and slightly smooth. The throat was injected. The heart was enlarged, the sounds were distant and of poor quality, and there was a pronounced gallop rhythm. There were no murmurs, and the blood pressure was 135 systolic, 100 diastolic.

Rules were prominent throughout the chest; the breath sounds were dull and distant at the bases, especially on the right. The abdomen was distended with fluid, and the liver was felt 4 to 5 cm below the costal margin. The tip of the spleen was questionably palpable. The lower legs were edematous. The left fourth and fifth terminal phalanges were missing.

The temperature was 97.6°F, the pulse 100, and the respirations 25.

Examination of the urine was negative. A blood Hinton test was negative. The blood nonprotein nitrogen was 25 mg per 100 cc. An electrocardiogram showed a PR interval of 0.21 second, with partial auriculoventricular block and a rate of 90. T₁ was low, T₂ and T₃ slightly inverted. The QRS complexes in Leads 1, 2 and 3 showed low voltage; those in Leads 2 and 3 were slurred and notched. R₄ was small. An x-ray film of the chest, taken with a portable machine, revealed a hazy, mottled dullness scattered over both lung fields. There was an old fracture of the left ninth rib, with an overgrowth of callus. The heart was prominent in the region of the left ventricle, the aorta was tortuous.

On the day after admission, the patient's temperature, pulse, and respirations rose to 99.8°F, 120 and 36, respectively. He became restless and delirious. He was quieted with sedatives, and the daily administration of digitalis was continued. The blood pressure on the fourth day was 105 systolic, 60 diastolic. He was given oxygen therapy and mercurial diuretics. On the fifth day, however, he began to fail, and that evening he very suddenly developed labored respirations and quickly expired.

DIFFERENTIAL DIAGNOSIS

DR. PAUL D. WHITE. This man was relatively young to have had so much heart disease of the coronary type. At forty two years of age, he may, however, have belonged in the rheumatic group.

The description of the precordial pain is not detailed enough. We may get more information later. We should like to know which came first on exertion, the precordial pain or the dyspnea. The pain could have been due to indigestion alone and as described is not diagnostic. The dyspnea on exertion cannot, however, be ascribed to indigestion; it might have been due to pulmonary disease or to myocardial weakness. If we had questioned him closely we might have found that the so-called "dyspnea" on exertion was really substernal oppression, that is, angina pectoris and not actual dyspnea. Such an error in interpretation is common. Hence I am a little doubtful about that symptom.

We learn that effort as well as eating induced

these pains that are not adequately described. It is characteristic of coronary insufficiency that angina pectoris is induced less by eating than by effort, but more by effort after eating than by effort on an empty stomach. If angina pectoris is induced by eating alone the coronary insufficiency is of high degree, and must be considered very serious. When very slight effort induces angina pectoris that fact too is an indication of severe coronary insufficiency. "Following one of these attacks, he developed dyspnea, which forced him to sit down." If dyspnea is associated with rapidly progressive coronary disease then there must also be cardiac dilatation and failure. We do not see congestive heart failure from coronary disease alone unless there is actual occlusion, usually with myocardial infarction. We do not encounter coronary disease with appreciable cardiac enlargement unless there is actual thrombosis and infarction, but in such cases the heart can get very large without hypertension.

There is no statement as to whether he had convulsions during syncope—probably not. Apparently he had not fainted before this. On top of the other symptoms this is strongly suggestive of Adams-Stokes attacks, which are due primarily to the effect of extensive coronary disease on the conduction system of the heart. Apparently these were not just nervous fainting spells. We do not really know, however, whether the syncope was due to collapse from fatigue or hunger or whether he was having a real Adams-Stokes syndrome or even an excessive reaction to angina pectoris, the so-called "syncope anginosa."

"Six weeks before entry orthopnea appeared which on a few occasions forced him to sit upright in a chair throughout the night." That makes the dyspnea significant, and means that we can rule out asthma and other such factors, and that there was myocardial failure, that is, left ventricular failure, which can quickly follow coronary occlusion even though there has been no prolonged pain, as in this case.

"... he developed ankle edema. . . ." The right ventricle was doubtless failing, although he might have had a bilateral leg phlebitis to explain such ankle edema. If the edema were one sided we might say phlebitis, but on the basis of bilateral edema and the previous history of dyspnea we should diagnose failure first of the left ventricle and then of the right. "He was seen by a physician one week before entry, who prescribed a 'pill' of digitalis three times a day. . . ." This was seven weeks after his illness began. The digitalization was very mild.

A big question is, Why did he have these pains radiating up the arm to the heart? Were they

associated with the finger injury or did they come as the result of walking uphill. In other words, he might have had some angina pectoris for a year before this final illness. Is there any statement about what activity produced the pain? The history is very vague on this point. Angina pectoris could start in this way as well as in any other way. The paragraph about the past history seems wholly unimportant unless these pains in the arm were brought on by effort.

In the physical examination we find gallop rhythm, heart sounds of poor quality, and slight diastolic hypertension which perhaps is not important and might have been temporary. Rales were prominent not just at the bases but generally—perhaps due to pulmonary edema or emphysema. The dulling of the breath sounds was undoubtedly due to hydrothorax.

We have not enough evidence to indicate a bacterial endocarditis complicating the picture. The spleen may have been congested, although we do not usually feel it in case of simple congestive heart failure.

"The temperature was 97.6°F." If he was dyspneic, we should know the rectal temperature. He may have had pulmonary infection or infarction.

The electrocardiogram backs up the suggestion of the Adams-Stokes attacks previously mentioned, although not strongly. It is also in accord with the diagnosis of posterior myocardial infarction, since heart block and changes in T₂ and T₃ are quite characteristic of early infarction due to occlusion of the right coronary artery or the circumflex branch of the left coronary artery supplying the basal portion of the heart. Low voltage is a characteristic coronary-disease finding. The QRS complexes are typically coronary. With low voltage in a normal person you do not have changes in the T waves. Also there was a very small R wave in Lead 4. Heart block of severe grade in coronary disease due to thrombosis of the right coronary artery or the circumflex branch of the left coronary artery may be temporary. I have seen it last a day or two, and then disappear, with a return to normal rhythm.

There was not much fluid at the lung bases, according to the x-ray film. There was increase in the hilar markings of the lungs. The heart was large, deep as well as wide. There was no marked bulging of the pulmonary artery or marked prominence of either auricle.

Although the diastolic blood pressure went down from 100 to 60, he certainly was not any better. Whether this drop was associated with failure I do not know. He may have had further difficulties in the circulatory state as the result of pulmonary complications.

Terminal pulmonary infarction or infection is the best bet as a part of the final story during the last day or two. The whole illness of about two and a half months raises a strong suspicion of coronary involvement, with rapid progression. The cardiac death suggests a sudden accident and not hypertensive or rheumatic heart failure, cardiovascular syphilis or some very rare kind of heart disease, although they are possibilities. There is no evidence of a congenital abnormality. The case suggests coronary disease, even though the onset is not the usual one for coronary thrombosis, nor an absolutely typical one for angina pectoris. The history of symptoms is not, however, adequate. The electrocardiogram suggests basal myocardial infarction and failure of the myocardium, and the early death suggests infarction or infection of the lungs. I cannot see that there is anything but coronary disease from beginning to end, except for a terminal complication, and I should expect to find an infarct at the left lung base.

DR. HOWARD B. SPRAGUE: I saw the patient with Dr. William B. Breed. It was difficult to get a history because he was so sick, but I made the note that he probably had been dyspneic for two years because he told me he had had trouble in going up stairs during that time. I was unable to fit the case into any very clear category. My note was as follows:

Very interesting and, to me, obscure case. Rheumatic heart disease seems out, as does syphilitic heart disease, unless it is an acute myocarditis. He has probably been dyspneic for two years. The heart is enlarged, and there is a gallop rhythm. The electrocardiogram shows no evidence of previous hypertension. Coronary occlusion is not proved, and there is no evidence for pericardial disease. If this is not a case of diffuse coronary disease, as suggested by the low-voltage electrocardiogram, it is probably the rare one of a big heart of unknown etiology which cannot be diagnosed even at autopsy.

DR. WHITE: I may be making too much of the fainting attack and the solitary prolonged PR interval. I do not recall whether fainting occurs in heart disease of unknown etiology. I may be paying too much attention to the symptoms of heart pain and syncope.

CLINICAL DIAGNOSES

Cardiac hypertrophy, idiopathic.
Congestive failure.

DR. WHITE'S DIAGNOSES

Coronary heart disease, with posterior (basal) myocardial infarction.
Cardiac enlargement.
Congestive heart failure.
Pulmonary congestion and infarction (terminal).

ANATOMICAL DIAGNOSES

Cardiac hypertrophy and dilatation (idiopathic?).
Cerebral infarct, right occipital lobe.
Pulmonary embolism.
Pulmonary infarction, right.
Cortical infarct of kidney, recent.
Thrombosis of popliteal vein.
Chronic passive congestion: lungs, liver, spleen and kidneys.
Hydrothorax, bilateral.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: The heart weighed 425 gm. It was not so hypertrophied as one might expect, but the right auricle and ventricle were dilated to about twice normal size. Examination of the myocardium showed no evidence of infarction or even fibrosis. The cavities contained no mural thrombi, and the valves were perfectly normal. We examined the coronaries very carefully but found no significant amount of coronary disease. There was a little atheroma here and there, but certainly not more than one would expect in a man of forty-two. Microscopic examination of the myocardium did not add very much. There was very little scarring. The prominent feature of the microscopic examination was the marked fibrosis and thickening—in places up to a millimeter in depth—of the endocardium. This endocardial lesion has been described occasionally in congenital idiopathic hypertrophy in infants. We looked very carefully for Aschoff nodules and other stigmas of rheumatic disease in the myocardium and could not find any. So far as the heart is concerned we certainly can say that it does not represent a case of coronary or rheumatic heart disease.

DR. WHITE: Did the microscopic examination of the myocardium show fibrosis?

DR. CASTLEMAN: Practically none. We cut several sections of the heart muscle in various places, and the only positive finding was the scarring of the endocardium.

DR. WHITE: On both sides?

DR. CASTLEMAN: No; almost all on the left side. We also hunted for glycogen in the myocardium and found only a normal amount, certainly not what you would see in von Giercke's disease. The lungs showed chronic passive congestion and one small, fairly old infarct in the right middle lobe. The source of the embolus that caused this infarct was a thrombus in the popliteal vein. There was also an old infarct in the left kidney, which if I recall correctly was also true of some of these cases of cardiac hypertrophy

of unknown etiology in adults that Levy* reported. I believe he found small thrombi in the interstices of the heart muscle as the source of the emboli.

DR. WHITE: What was the thickness of the heart wall?

DR. CASTLEMAN: The right was 5 mm., the left 15 mm.; this points to a little hypertrophy on both sides. I do not believe that we can rule out hypertension, since he was in heart failure and we do not know what the blood pressure was before admission.

DR. WHITE: It was not a big enough heart for hypertension alone.

DR. CASTLEMAN: At least one of the fainting spells can be explained by the presence of a recent large infarct in the right occipital lobe of the brain. In addition, recent small hemorrhages were scattered over the surface of the brain.

DR. SPRAGUE: The pulmonary circulation was entirely negative as I remember. You ruled out intrinsic disease there?

DR. CASTLEMAN: Yes.

CASE 26402

PRESENTATION OF CASE

A seventy-nine-year-old man entered the hospital complaining of shortness of breath.

The patient was first seen in the Out Patient Department where he stated that he had noticed an increasing shortness of breath, accompanied by substernal constriction on exertion, for the past six months. In the past three months he had been compelled to rest frequently while walking. During the last few weeks he awakened at night dyspneic and unable to take a full breath; this was relieved by sitting up. In addition the patient had had an aching pain in the region of the left sacroiliac joint which radiated down the left thigh and was unrelated to motion. This had been present for two years and had increased of late to the extent that it required "dope" for relief. In general he felt weak and had lost 19 pounds in the last four months.

In the past he had suffered from gonorrhea at eighteen and typhoid fever at fifty-four years of age. Urethral strictures had been dilated by sounds two years before. His father died at sixty-eight of "kidney trouble," and his mother of tuberculosis at forty.

On physical examination the patient was alert and appeared well. The heart was enlarged to the left anterior axillary line. The rhythm was regular, the sounds of good quality; no murmurs were heard. The blood pressure was 180 systolic, 95

diastolic. There were a right inguinal hernia and diastasis recti abdominis. A firm, tender, rounded and fusiform mass about 6 cm. in diameter was palpable in the left mid-abdomen. It pulsated and did not move with respiration. Rectal examination was negative, and the prostate not enlarged.

The temperature and respirations were normal, and the pulse between 80 and 100.

Examination of the urine was negative. A white-cell count was 10,000. A blood Hinton test was negative.

X-ray films of the chest showed the heart to be enlarged in the region of the left ventricle. The abdominal aorta was extensively calcified, and the calcium appeared to expand in a fusiform bridge between the first and fourth lumbar vertebrae to the left of the spine. Electrocardiographic recordings showed partial auriculoventricular block, blocked premature auricular beats and nodal escape. Lumbar puncture and cerebrospinal-fluid Wassermann tests were negative.

The patient was placed on digitalis and aminophyllin. He improved under this treatment and when he restricted his activity remained free from dyspnea and substernal distress. The seventh week after he had come under observation he began to have attacks of left-upper-quadrant pain of unstated character, associated with shortness of breath and requiring a hypodermic for relief. The only addition to the clinical findings at this time was pitting edema of the ankles. One month later he was admitted to the hospital for observation and study of the abdominal mass. The day after entry the patient walked into the lavatory and was found dead a few minutes later.

DIFFERENTIAL DIAGNOSIS

DR. HOWARD B. SPRAGUE: This man survived almost to the age of eighty years, so that he probably succumbed to the changes that are due to the passage of time, and one thinks at once of arteriosclerosis and cancer. He had a relatively short history of what appears to be cardiovascular difficulty with shortness of breath. It is a little difficult to be sure whether this shortness of breath can be called evidence of congestive failure or whether the breath was cut off when he exerted himself and therefore was an anginal manifestation. However, there was substernal constriction on exertion, a fact that suggests angina pectoris. He also was having nocturnal attacks of dyspnea, relieved by sitting up, and finally pain in the left sacroiliac region radiating down the left leg. The story of weight loss at this age is not necessarily of any significance except that it may go with arteriosclerosis. He had had gonorrhea when he was young; he had had typhoid fe-

*Levy, R. L., and Rousslet, L. M.: Cardiac hypertrophy of unknown etiology in young adults. *Am. Heart J.* 9:178-196, 1933.

ver. Typhoid fever has been blamed by some physicians for subsequent vascular changes, but if it was a factor, it took a long time with this man. The examination showed that he was alert and appeared well, an observation that is quite consistent with the story that his troubles were largely of a paroxysmal or episodic nature. He had to exert himself in order for symptoms to appear, or be awakened in the night with symptoms. He had a large heart extending to the left axillary line. The rhythm was regular, and the sounds of good quality; there were no murmurs. There seems to have been no evidence of valvular disease. He had moderate systolic hypertension, and a mass in the abdomen.

You have heard the report of the x-ray examination. You can see the calcification that was described in the wall of the aorta. The heart does not appear so large as the physical examination suggested. There is nothing suspicious in the thoracic aorta.

DR. PAUL D. WHITE: Is the aortic calcification in the region of the palpable tumor?

DR. SPRAGUE: I judge that it was because it extends from the first to the fourth lumbar vertebra and it was noted that the tumor was in the mid-abdomen. It was just about opposite this point, which I should judge to be the position of the umbilicus, and the dilatation would extend from the level of the ribs to that of the ilium.

The electrocardiogram is abnormal chiefly because of the occurrence of partial auriculoventricular block. All attempts to demonstrate serological evidence of syphilis in this man were unavailing, including a blood Hinton test and a spinal fluid Wassermann test. He improved under the treatment but entered the hospital to have the tumor mass studied. He showed at that time some pitting edema of the ankles, which might be further evidence of congestive failure, although it might also have been due to some obstruction higher up in the veins or lymphatics interfering with drainage from the legs. He died very suddenly.

The question that concerns us chiefly, I think, is what the abdominal mass had to do with his death. You remember last week we had a case of syphilitic aortic aneurysm showing marked calcification in its walls. They certainly describe here what appears to be a dilatation of the abdominal aorta with calcification in the walls. It is a fusiform affair, not sacular. It seems to me, however, it could be responsible for the referred leg symptoms and conceivably the cause of the vague attacks of left-upper-quadrant pain. The calcified fusiform bridge at the upper end of the

mass was apparently in or close to the left upper quadrant, and this mass extends nearly the whole length of the side of the abdomen and could cause pressure, perhaps involving several nerve pathways. There does not seem to be any evidence by x-ray of erosion of any of the vertebrae.

I think that we shall have to consider that this is an aneurysmal dilatation of the aorta, and the question is whether it is on a syphilitic or on an arteriosclerotic basis. Abdominal aneurysms are difficult to diagnose and have been picked up here at autopsy entirely unsuspected and causing no symptoms. So far as the syphilitic background is concerned I might give you some figures that I collected this spring about our experience here with aneurysm of the aorta. In 28 cases of aneurysm of the aorta proved to be syphilitic at autopsy between 1908 and 1938, there were 15 in which Wassermann tests alone were done and in 3 of these the test was negative; there were 5 in which the Hinton test alone was done, and in 2 of these it was negative; and there were 8 in which both tests were done, and none of these would have been missed. In a series of 23 private cases of syphilitic aortitis 20 had positive serological tests. We have here two types of test,—blood and spinal fluid,—and both were negative. We have an old man who gave us a story of gonococcal infection, and yet we can only guess about any syphilitic background, with possible calcific changes. He had, I believe, hypertensive and coronary heart disease with angina pectoris. He died suddenly, and we need no other diagnosis to explain the sudden exitus.

We have not, it seems to me, sufficient evidence to suspect that there was a rupture of the dilated abdominal aorta, although the history just before the patient was admitted to the hospital included pains in the left upper quadrant that suggest some stretching or early subacute rupture of a dilated aorta. I am going to guess, then, that he showed coronary arteriosclerosis and that he probably died of angina pectoris, in which case one would not necessarily expect to find a fresh thrombus occluding a vessel. He may very well have had fluid blood in the coronary arteries. There was a diffuse arteriosclerotic process in the aorta. I should not be surprised if he had more than one aneurysmal dilatation in the aortic tree or even in the large vessels. I vote against syphilis in this case, and I find no reason to suspect that this was a dissecting aneurysm such as we see in the thoracic aorta, for the reason that he gave no story of the acute attack of pain that would have accompanied a true dissection and because dissecting aneurysm is a disease of the thoracic aorta which dissects into the abdominal aorta.

DR. BENJAMIN CASTLEMAN: Dr. White, have you any comments?

DR. WHITE: No, except to say that the death in the lavatory is a very important point so far as the hazard of constipation is concerned in a patient with angina pectoris. I wonder if there was any story of straining at stools. Was there any note of constipation?

DR. SEDGWICK MEAD: Not that I recall.

DR. WHITE: I have occasionally advised such patients if they are constipated to take tablets of nitroglycerin just before defecation.

DR. CASTLEMAN: The commonest cause of death occurring in the lavatory in this hospital is massive pulmonary embolism.

DR. MEAD: The complaint that this patient had on entry to the hospital was a very severe pain radiating down the lateral aspect of the left leg. The cardiac symptoms were more or less under control from the previous digitalization. The abdominal mass was distinctly more prominent on the left than on the right; it was high enough so that a surgical consultant thought that it was perhaps an aneurysm of the splenic artery.

CLINICAL DIAGNOSES

Ruptured, arteriosclerotic, abdominal aortic aneurysm.
Hypertension.
Hypertensive arteriosclerotic heart disease, with coronary sclerosis.
Angina pectoris.
Right inguinal hernia.

DR. SPRAGUE'S DIAGNOSES

Hypertensive and coronary heart disease.
Coronary sclerosis, with angina pectoris as cause of death.
Arteriosclerotic abdominal aneurysm, with questionable subacute perforation.

ANATOMICAL DIAGNOSES

Aneurysm of abdominal aorta, syphilitic, with rupture.
Retroperitoneal hematoma and ecchymoses.
Hemoperitoneum.
Arteriosclerosis, marked aortic and coronary.
Coronary occlusion, old.
Cardiac infarct, localized, healed?
Cardiac hypertrophy, hypertensive type.
Nephritis, chronic vascular.
Emaciation, slight.

Prostatic hyperplasia.
Diverticulosis coli.
Perisplenitis, chronic.
Cholecystitis, chronic.
Cholelithiasis.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: At autopsy we found a heart that weighed 500 gm. and showed no disease of any of the valves. The coronary arteries were sclerotic and calcified, the lumen of the main right branch being reduced to a pinpoint opening by an old thrombus. There was patchy scarring of the myocardium, with one fairly large scar that apparently was the result of the old thrombotic process.

DR. WHITE: Where was that?

DR. CASTLEMAN: That was on the posterior wall of the left ventricle near the septum. If the autopsy were limited to just those findings we would have concluded that the man died of angina pectoris. However, abdominal examination showed rupture of a tremendous aneurysm which rose from the anterior wall of the aorta 7 cm. above the bifurcation. The aneurysm itself measured about 8 cm. in length and contained an organized mural thrombus. At the time of autopsy we were all agreed it was probably an arteriosclerotic aneurysm because of the marked calcification. Sections, however, showed fairly good evidence of syphilis—lymphocytic infiltration around the vasa vasorum of the media and adventitia, and destruction of elastic tissue. The ascending aorta was arteriosclerotic throughout.

The blood that had escaped from the aneurysm formed a hematoma in the retroperitoneal tissues, which in turn had ruptured into the peritoneal cavity and pelvis.

DR. WHITE: I should like to add another word with respect to my recent experience with arteriosclerotic thoracic aortic aneurysms in aged people. Abdominal arteriosclerotic aortic aneurysms have been much commoner than have thoracic aneurysms. My attention was called to the thoracic type a few years ago because of an experience with two very old ladies both of whom had been known to have aneurysmal dilatation of the aorta with no evidence of syphilis and both of whom died of rupture of the aneurysm, one with dissection and one without dissection but with multiple aneurysms. Autopsy confirmed the arteriosclerotic nature of the aneurysms in both cases.

The New England Journal of Medicine

Formerly the
Boston Medical and Surgical Journal
Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE
ON PUBLICATIONS

Official Organ of

THE MASSACHUSETTS MEDICAL SOCIETY
THE NEW HAMPSHIRE MEDICAL SOCIETY
THE VERMONT STATE MEDICAL SOCIETY

EDITORIAL BOARD

Joseph Garland M.D.	John P. Sutherland M.D.
Willam B. Breed M.D.	Stephen Rushmore M.D.
George R. Minot M.D.	Henry R. Viets M.D.
Frank H. Lahey M.D.	Robert M. Green M.D.
Sheldon Warren M.D.	Charles C. Lund M.D.
George L. Tobey Jr. M.D.	John F. Fulton M.D.
C. Guy Lane M.D.	A. Warren Stearns M.D.
William A. Rogers M.D.	Dwight O'Hara M.D.

ASSOCIATE EDITORS

Thomas H. Lanman M.D.	Donald Munro M.D.
Henry Jackson Jr. M.D.	
Walter P. Bowers M.D.	EDITOR EMERITUS
Robert N. Nye M.D.	MANAGING EDITOR
Clara D. Davies	ASSISTANT EDITOR

SUBSCRIPTION TERMS: \$6.00 per year in advance postage paid for the United States; Canada \$7.82; Boston (including war exchange tax) per year \$5.57 per year for all foreign countries below, according to the Postal Union.

MATERIAL for early publication should be received not later than noon on Saturday.

THIS JOURNAL does not hold itself responsible for statements made by any contributor.

COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston, Massachusetts.

UNITED STATES MARINE HOSPITAL AT THE PORT OF BOSTON

A NEW chapter in a long and honorable history was written on Thursday, June 7, 1940, when the sixth home of the United States Marine Hospital, the oldest hospital in Massachusetts, established in 1799, was dedicated in Boston. For almost one hundred and forty-two years this establishment has furnished medical care to seamen and, in recent years, to government employees not members of the uniformed services. Dr. Thomas Parran, surgeon general of the United States Public Health Service, and the Honorable Paul V. McNutt, federal security administrator, addressed the gathering at the dedication, both pointing out in their remarks that the public health program of the federal government was in its own way as important as the national defense program.

To many the Marine Hospital has been, as a matter of fact, frequently confused with the Naval Hospital whose neighbor it was in Chelsea. An act

of Congress, signed in July, 1799, by Massachusetts's own John Adams, provided for the "relief of sick and disabled seamen," and the first marine hospital in the United States was opened in temporary quarters on Castle Island (then Castle William) in South Boston. Only three hospitals in the United States are older than the Marine Hospital at the Port of Boston—the Pennsylvania Hospital at Philadelphia (1752), the Charity Hospital of Louisiana at New Orleans (1784) and the New York Hospital at New York City (1791).

The masters of sailing vessels were, in the early days of the nineteenth century, authorized to deduct certain sums each month from the pay of seamen, which were paid into a fund used to support this and other marine hospitals along the Atlantic coast. Thus present day plans for compulsory health and sickness insurance were anticipated by more than a century. The administration of these contributions and the general oversight of the Marine Hospital resided in the office of Secretary of the Treasury, where it remained until July 1, 1939 when it was transferred to the Federal Security Agency. The contributions by seamen were continued until 1884, when expenses so far outran contributions that the assessments were discontinued and the cost of hospital maintenance was met by levying a tonnage tax on foreign vessels. In a short time this tax was found to be greater than necessary, and the money was paid directly to the United States Treasury, which in turn paid hospital costs from its general funds.

All these facts and many others about the hospital's one hundred and forty-two year story can be learned from a pamphlet entitled *The United States Marine Hospital at the Port of Boston, 1799-1940*, by William John Trask, its medical director from 1935 to 1940. Benjamin Waterhouse, Hersey Professor of the Theory and Practice of Physic at Harvard Medical School from 1783 to 1812, was an early director, and under his leadership an outpatient department was initiated. Today this department is one of the most active in the hospital and provides treatment for almost seven times the number of patients who are hospitalized. The house patients in 1810 numbered 242, and in 1812 totaled 649, due to the casualties of the war

then being waged. British prisoners and seamen from the frigates *Constitution* (after her battle with the *Guerrero*) and *Congress*, from merchant vessels and from the clippers in the China trade, all received the finest care available at the time. In the early days it was the custom for sailors to be brought directly to the hospital, many in extremis because of the delay in treating injuries before hospitalization. Today the Coast Guard and Public Health Service, with the cooperation of the staff of the Marine Hospital, send advice in regard to the treatment of seamen aboard ship via radio telephone, and when the need is dire the patient is brought to the hospital by airplane or speedy motorboat.

For the accomplishments of his predecessors and their staffs Dr. Trask has spared no praise. For his own work he is overmodest. It was his keen insight into the problems of the hospital and its physical limitations when he took up his duties, as well as his earnest planning, that is chiefly responsible for the new plant at Brighton. Dr. Grover Kempt, well known for his experience in public-health administration, has been selected to succeed Dr. Trask and is assuming the duties of directing this hospital in the new phase of its development. With an energetic and well-trained full-time staff and an excellent group of consultants who represent all the specialties, its services are not surpassed by the finest general hospitals in the country. In the early years of its existence the hospital was a teaching unit of Harvard Medical School, and this function is continued in a slightly different form at the present time, chiefly by means of intern training. In the past, research facilities have been necessarily limited by the demands for ward space; in the new building provision has been made for this purpose, and a number of specific research projects are being planned.

The United States Marine Hospital at the Port of Boston represents and typifies the "American way" in medicine: for nearly one hundred and forty-two years it has maintained a high tradition of service to men who go down to the sea in ships. With new facilities it looks forward to long continuance and expansion of its service as one of the leading, although not the largest, government-operated hospitals in the Western hemisphere.

CHILDHOOD MORTALITY

A RECENT *Statistical Bulletin* of the Metropolitan Life Insurance Company, comments favorably on the reduction of mortality in childhood during the last three decades. Today the mortality in the ages from one to fourteen years is only a fifth of that less than thirty years ago. In 1939 there were only 13 deaths per 1000 insured white children of these ages as compared with a rate of 64 in 1911.

A number of gains are responsible for this remarkable improvement. Influenza and pneumonia, heading the list in 1911, with a death rate of 100 per 100,000, rose to an all-time high during the pandemic of 1918 with a rate of 345 but dropped to less than 21 in 1939; the latter figure is below the rate for total accidents, and thus drops this cause of death from first into second place.

Diphtheria, second in the list in 1911 with a rate of 88 per 100,000 children, dropped to 4 in 1939. The other three principal communicable diseases of childhood registered similar, though less spectacular, drops: scarlet fever from 41 to 2, measles from 36 to 2, and whooping cough from 20 to 2. Diarrhea and enteritis were in third place in 1911, but the death rate of nearly 65 dropped to 4 in 1939, during the corresponding period the rate for tuberculosis fell steadily from 45 to less than 6.

Acute rheumatic fever, nephritis and organic heart disease dropped to a third or a quarter of their original rates; all fatal accidents fell from 57 in 1911 to 26 in 1939. Deaths from appendicitis have shown no improvement, remaining at about 10 per 100,000, and consequently this cause of death moved from eleventh place in 1911 to third place in 1939. Deaths from automobile accidents are the only ones to show an increase,—from less than 3 in 1911 to over 10 in 1939,—and they now stand second only to those from influenza and pneumonia. Even this figure, however, shows a substantial reduction from the maximum rate of 18 in 1929.

These figures are indicative of the slow but steady advances that humanitarian science has made in ameliorating the condition of mankind. It is a sad commentary on modern civilization that such hard-won gains can be so rapidly reversed by other causes.



ALEXANDER SWANSON BEGG

1881-1940

It is with a deep sense of loss that the *Journal* records the sudden death of the secretary of the Massachusetts Medical Society. For five years he had faithfully and effectively fulfilled the exacting and arduous tasks of this office.

Dr Begg was best known, however, as an able contributor to the advancement of medical education. He enjoyed expending the major part of his unexcelled energy in this field. He started medical teaching at his alma mater, Drake University, and continued this activity at Harvard University and at Boston University, where he had been professor of anatomy for nineteen years. For the past seventeen years he was the energetic and respected dean of Boston University School of Medicine.

His activities outside of the medical school were many and varied. He was widely known for his two year service in the Medical Corps of the United States Army during World War I. For eleven months he commanded Base Hospital 88 in France, having advanced from the rank of lieutenant to that of lieutenant colonel. Since then he participated actively in the Medical Reserve Corps in the New England area, holding the rank of colonel in the Auxiliary Corps, United States Army. In the past he served on the Executive Council of the Association of American Medical Colleges, as chairman of the Committee on Education of the Association of American Medical Colleges, as president of the Norfolk District Medical Society of the Massachusetts Medical Society and as a director of the Boston Chamber of Commerce and chairman of its Committee on Public Health. At the time of his death he was Massachusetts chairman of the Committee on Medical Preparedness of the American Medical Association, on the editorial board of the *Diplomate* and chief examiner of the Boston Subsidiary Board for the Part III examinations of the National Board of Medical Examiners.

He was a member of the American Association for the Advancement of Science, the American Association of Anatomists, the Association of Military Surgeons, the American Medical Association and Phi Beta Kappa.

Those who realize the significance of the distinctive ability with which the duties of these positions were fulfilled, as well as the many who were privileged to benefit intimately from his helpful guidance, generosity, good humor and friendliness, are convinced that Dr Begg's leadership in medical education and other matters relating to the medical profession will not soon be forgotten.

SATURDAY, OCTOBER 12

*9-10 a. m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*Open to the medical profession.

OCTOBER 6-11 — Annual meeting of the American Academy of Ophthalmology and Otolaryngology. Page 81, issue of July 11.

OCTOBER 8-11 — American Public Health Association. Page 655, issue of April 11.

OCTOBER 9 — Four County Medical Society. Page 520, issue of September 26.

OCTOBER 10 — Pentucket Association of Physicians.

OCTOBER 10-MAY 15 — United States Naval Hospital. Page 558.

OCTOBER 11, 12 — Pan American Congress of Ophthalmology. Page 898, issue of May 23.

OCTOBER 14-25 — 1940 Graduate Fortnight of the New York Academy of Medicine. Page 305, issue of August 22.

OCTOBER 15 — South End Medical Club. Page 558.

OCTOBER 16 — Waltham Medical Meeting. Page 558.

OCTOBER 21 — American Board of Internal Medicine. Page 369, issue of February 29.

NOVEMBER 13, 14 — New England Postgraduate Assembly. Cambridge, Massachusetts.

DECEMBER 27-29 — National Convention of the Association of Medical Students, Boston.

JANUARY 4, 1941 — American Board of Obstetrics and Gynecology. Page 1044, issue of June 20.

MARCH 8 — American Board of Ophthalmology. Page 201, issue of August 1.

APRIL 21-25 — American College of Physicians. Page 1065, issue of June 20.

JUNE 2-6 — American Medical Association. Cleveland, Ohio.

DISTRICT MEDICAL SOCIETIES

SUFFOLK

NOVEMBER 7 — Censors' meeting. Page 305, issue of August 22.

WORCESTER

OCTOBER 9 — Rutland State Sanatorium, Rutland.

NOVEMBER 13 — Grafton State Hospital, Grafton.

DECEMBER 11 — St. Vincent Hospital, Worcester.

JANUARY 8, 1941 — Worcester City Hospital, Worcester.

FEBRUARY 12 — Worcester State Hospital, Worcester.

MARCH 12 — Memorial Hospital, Worcester.

APRIL 9 — Hahnemann Hospital, Worcester.

Supper will be served at 6 30 p. m. followed by a business meeting and entertainment program.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Manual of the International List of Causes of Death: As adopted for use in the United States. Based on the Fifth Decennial Revision by the International Commission, Paris, October 3-7, 1938. *Manual of Joint Causes of Death.* Fourth edition. Prepared under the supervision of Halbert L. Dunn, M.D., chief statistician for vital statistics. 8°, cloth, 452 pp. Washington: Government Printing Office, 1940. \$1.25.

Management of the Cardiac Patient. By William G. Leaman, Jr., M.D., assistant professor of medicine in charge of the Department of Cardiology, Woman's Medical College of Pennsylvania, Philadelphia; cardiologist, Woman's College, Memorial Hospital and Northeastern Hospital for Contagious Diseases; consulting cardiologist, St. Luke's and Children's Hospital, Philadelphia. 8°, cloth, 705 pp.,

with 255 original illustrations and 29 tables. Philadelphia: J. B. Lippincott Company, 1940. \$6.50.

Food, Nutrition and Health. By E. V. McCollum, Ph.D., Sc.D., professor of biochemistry, and J. Ernestine Becker, M.A., associate of biochemistry, School of Hygiene and Public Health, Johns Hopkins University, Baltimore, Maryland. Fifth edition, entirely rewritten. 12°, cloth, 127 pp. Baltimore: privately printed, 1940. \$1.50.

The International Clinics: Original contributions, clinics and evaluated reviews of current advances in the medical arts. Edited by George Morris Piersol, M.D., professor of medicine, Graduate School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania. Vol. III, New Series 3. 8°, cloth, 358 pp., with 87 figures, 17 tables and 14 charts. Philadelphia: J. B. Lippincott Company, 1940. \$3.00.

De morbis artificum, Bernardini Ramazzini, diatriba; Diseases of Workers. The Latin text of 1713 — revised, with translation and notes. By Wilmer Cave Wright, emeritus professor of Greek, Bryn Mawr College. 8°, cloth, 549 pp., with 3 illustrations. Chicago: University of Chicago Press, 1940. \$5.00.

BOOK REVIEWS

Albert Calmette, sa vie, son oeuvre scientifique. By P. Noël Bernard and Léopold Nègre. 4°, paper, 272 pp. Portrait. Paris: Masson et Cie, 1939. \$1.15.

This book, like Vallery-Radot's *Life of Pasteur*, should be in every medical student's library. Apart from the simple charm with which it is written, its appeal lies in the inspiration which can be gained by every enthusiastic scholar of medicine from the life of a great investigator and physician who was also a warm-hearted, adventurous human being.

In Calmette, as in so many great Frenchmen, the important influence of the broad, humanistic education of the *lycée* or government high school is apparent. It is interesting to record that his bachelor's thesis at the Lycée Saint-Louis in Paris dealt with the question, "In what does the philosophy of Leibnitz differ from that of Spinoza?" His boyhood ambition was to be a sailor. Eventually he compromised by becoming a naval surgeon and making several voyages to the Orient as assistant-surgeon. In Amoy he met Sir Patrick Manson, who was at that time carrying out his brilliant work on mosquitoes and filariae, and Calmette, who on his return to France wrote his doctor's thesis on filariasis, was undoubtedly deeply influenced by the great investigator. While in the East on these and subsequent voyages, Calmette gave evidence of his eager mind by studying anthropology, ethnology and native languages.

His desire to marry and settle down caused him to leave the colonial service in 1887, and the modesty of his demands on life is attested by his willingness to accept a living as government physician of the islands of St. Pierre and Miquelon. His idea was to provide a few years of calm, domestic solitude for his young wife and himself. But the instinctive investigator finds problems wherever he goes, and on these deserted islands Calmette began to study a disease of codfish, an investigation which brought him to the attention of Roux and of Pasteur. Through the latter he was soon offered the opportunity of establishing a laboratory for the production of smallpox and rabies vaccine at Saigon in Indo-China. The promptness of his acceptance of this distant post surprised even

Pasteur, but to Calmette it meant 'a chance to prove to himself whether he was capable of initiative or independent accomplishment.' This outline of his early life shows that Calmette was as adventurous physically as he was intellectually.

In Saigon, in 1891, he began his classical studies on snake venoms which, apart from their practical value, he came of fundamental significance in defining the principles of toxin-antitoxin reactions in general. Here, too, he worked on plague, made diphtheria antitoxin and carried out a large number of minor studies suggested by local problems. In 1894 he was recalled to France to become the director of the Pasteur Institute, of Lille, where he remained twenty-five years. His last service was that of assistant director of the Pasteur Institute, of Paris under his old teacher, Roux.

Calmette's greatest work was undoubtedly that on snake poisons. Next to that rank his studies on tuberculosis, too well known to the medical profession to require detailed discussion. In addition to these master studies he contributed extensively to water purification, to the prevention of hookworm disease and to general hygiene.

His story is told in this book with affection and great literary skill. It will keep him alive as one of the great figures of the post-Pasteurian period for the inspiration of young medical investigators.

Chemotherapy and Serum Therapy of Pneumonia By Frederick T. Lord, clinical professor of medicine, emeritus, Harvard Medical School, Elliott S. Robinson, director, Division of Biologic Laboratories, Massachusetts Department of Public Health, Roderick Heffron, medical associate, The Commonwealth Fund 8", cloth, 174 pp., with tables. New York: The Commonwealth Fund, 1940 \$1.00.

This small book has had an interesting career. It made its bow in 1936, a ninety-one page booklet with eleven illustrations and entitled *Lobar Pneumonia and Serum Therapy with Special Reference to the Massachusetts Pneumonia Study*. It achieved great popularity at once, because the therapeutic procedures for pneumonia recommended by its two authors, Drs. Lord and Heffron, were generally admitted as being sound, and the book was thoroughly readable.

A second edition appeared in 1938. The book was then called *Pneumonia and Serum Therapy*. While the title was shorter, its contents were longer—a hundred and forty-eight pages. Again, the book made a favorable impression on all who read it.

Now in 1940, two years after the second edition was printed, a third edition appears. Within the last two years a new title has become necessary, for chemotherapy has necessarily been added. A third author's name appears on the title page. The book has grown to be a volume of a hundred and seventy-four pages. Evidently the authors feel no need for many illustrations, because the third edition contains even less than did the first two. But the added length of the book reflects clearly what has happened to pneumonia in four years. Actually, as the contents of the book prove, nearly twice as much is now known of the treatment of pneumonia as was known in 1936.

Ever since the first edition was published the subject matter of the book has been well balanced. It continues to be simply and readably written, and it is a mine of authoritative information on pneumonia from men of wide experience with well balanced and properly critical minds. And, thank goodness, the book remains modest. In spite of its popularity, in spite of being bigger, bet-

ter and much more informative than it was, it gives itself no airs. It still sells at the original price.

On the whole, this small volume which so conveniently fits into one's pocket or bag should be a lifesaver. For, as it is stated in the opening sentence, pneumonia is a medical emergency. The life of the patient may depend on the early application of appropriate treatment. We New Englanders who know the treacherous side of pneumonia should be thankful for such a satisfactory volume.

Savill's System of Clinical Medicine Eleventh edition. Edited by Agnes Savill, M.D. and E. C. Warner, M.D., F.R.C.P. 8", cloth, 1141 pp., with 184 illustrations, 6 colored plates and 44 tables. Baltimore: William Wood & Company, 1939 \$9.00.

The eleventh edition of this textbook of medicine, originally compiled from personal experience over a generation ago by a British practitioner, T. D. Savill, for use by practitioners, continues to be built around the patient's cardinal symptom. The structural pattern of the book is the full description of the cardinal symptoms of each disease, as for example, chest pain in cardiac disease, followed by an enumeration and a less detailed discussion of all other conditions in which the particular symptom may occur. Apropos of this method, the author quotes Matthews Duncan, 'If you do not know of a thing you are quite sure not to suspect it, and in all cases of difficult diagnosis if you do not suspect the disease you are almost certain not to find it.'

It is a very informative work, written in a concise style, and well illustrated. As the emphasis is on making a correct diagnosis, a good part of the book is devoted to chapters which in America make up the textbooks on medical diagnosis. Although the anatomic and physiologic aspects of disease are clearly indicated, etiology is but briefly considered.

The arrangement of the material is rather archaic. Thus the diseases of the thyroid gland are included in a chapter entitled "The Upper Respiratory Passages and the Thyroid Gland." Diabetes mellitus, diabetes insipidus and Bright's disease are found in the chapter entitled "The Urine." The blood dyscrasias are considered in a chapter headed "General Debility, Pallor and Emaciation." There are chapters on the "Abdomen," "Diseases Peculiar to Women" and "Skin." At the end there is a useful prescription list.

It is a quaint, interesting work, which, judging from its popularity, must have proved useful to many practitioners.

The Hypothalamus and Central Levels of Autonomic Function Proceedings of the Association for Research in Nervous and Mental Disease. Volume XX, 8", cloth, 980 pp., with 319 illustrations and 35 tables. Baltimore: Williams & Wilkins Company, 1940 \$10.00.

This is the twentieth volume in a continuous series published under the auspices of the Association for Research in Nervous and Mental Disease. The annual meetings of this association, occurring in New York City in December of each year, have produced some of the best work on neurology and psychiatry in this or any other country. A single topic is considered during the two-day session, and the meeting for 1939 was no exception to the general rule. The subject of the hypothalamus was particularly important, for a large number of facts have resulted from extensive investigations of this single center of the brain in recent years.

While a complete review of a book of this character

cannot be given, it should be noted that the volume covers the anatomy and physiology of the hypothalamus as well as the clinical symptoms associated with dysfunction of this part of the brain. There is an excellent historical résumé of the subject by the chairman of the editorial board, Professor John F. Fulton, and Fröhlich's original paper on a tumor of the hypophysis, dated 1901, written in German and illustrated, is reprinted. It is interesting to know that Fröhlich's patient is still living.

This volume forms the most complete review of the subject ever presented in print and, as such, is an outstanding contribution to medicine. The papers are of a high order, and the illustrations and charts clear and adequate. There are an extensive bibliography, an index and a list of the members of the association.

Congenital Cleft Lip, Cleft Palate and Associated Nasal Deformities. By Harold Stearns Vaughan, M.D., D.D.S. 8°, cloth, 210 pp., with 259 illustrations. Philadelphia: Lea & Febiger, 1940. \$4.00.

During the last few years considerable literature on cleft-palate surgery has appeared, and much progress has been made in this field. This is evidenced by the quality of the work that we see at the present time. Although some of the operations have become standardized, there is not as yet a unanimity of opinion regarding many of the pressing problems in cleft-palate surgery. In this book, the author has outlined his methods of approach based on his vast experience in this field. His main purpose is "to evaluate the various methods and to make the book of practical value to the general surgeon, to the pediatric surgeon and to the specialist in plastic and reconstructive surgery." On the whole, he has succeeded in his purpose, as the book is well illustrated with photographs and diagrams of the various operative procedures. The chapters on the primary closure of split lip and palate are dealt with more thoroughly than those on secondary repairs and late deformities in cleft-palate patients. The last two chapters dealing with orthodontic treatment and prosthetic restoration are a valuable addition, although one wishes that the subject could have been discussed in greater detail.

Whether for detailed information or for reference this book serves a very useful purpose.

Minor Surgery. By Frederick Christopher, S.B., M.D., with a foreword by Allen B. Kanavel, M.D. Fourth edition. 8°, cloth, 990 pp., with 639 illustrations. Philadelphia: W. B. Saunders Company, 1940. \$10.00.

Few books are of such intense practical value to the general practitioner as this one. It emphasizes the importance of trivial injuries, and constitutes a competent and handy consultant on many of the minor conditions which so often are emergencies.

The author has recognized the difficulty of naming this work so that the title will cover adequately the many conditions described. Burns, injuries, tumors and carbuncles cannot well be lumped under any single heading. The important point is that this volume prescribes for conditions which are too often only mentioned in ordinary medical and surgical works because of their obviousness or seeming insignificance.

Some will find the editorial style difficult at first, for the varied opinions of many writers are summarized without attempt at critical analysis. But if sharp decision is somewhat lost by this method, the reader is placed in a position to choose from several methods. One physician often finds a certain therapy to work better in his hands

than others; and where a choice is presented as to treatment, one form may be more readily available than another.

There is a need for all types of textbooks, but their usefulness varies widely. This one will be well thumbed by any practitioner who has it in his library.

Clinical Toxicology. By Clinton H. Thienes, M.D., Ph.D. 12°, leather, 309 pp., with 7 illustrations. Philadelphia: Lea & Febiger, 1940. \$3.50.

The advent of and rapid advances in chemotherapy have focused attention on the various toxic effects of all the drugs now in daily use as well as the more uncommon ones. This small book encompasses a surprisingly large amount of material condensed in a highly utilizable form. It is evident that in the choice of material the pharmacological literature was carefully scrutinized.

The reviewer believes that a daily dose of 30 mg. of amphetamine (Benzedrine) sulfate is rather high to be regarded as within the therapeutic limit, except in some cases of narcolepsy, which today represent only a small percentage of the cases in which the drug is used. Parathormone is sometimes used in the treatment of lead poisoning; hence its toxic effects should be mentioned. Cholinergic and adrenergic are now accepted terms. The toxic effects of ethyl gasoline deserve consideration, as well as those following the administration of excessive amounts of water. Unquestionably, in future editions sulfanilamide and its related compounds will find inclusion. With these few exceptions the author has covered the subject very adequately.

Syphilis. Edited by Forest Ray Moulton, Ph.D. 4°, paper, 193 pp. Lancaster, Pennsylvania: The Science Press, 1938. \$2.50.

This symposium on syphilis, presented by the Section on the Medical Sciences of the American Association for the Advancement of Science, maintains the high standard expected of this eminent association on a subject which has so recently been lifted out of its relative obscurity into the dazzling light of popularity. The contributors are all unquestioned authorities in their particular fields. The various phases of syphilis that are covered in this collection of papers are of a definitely wider range than is usually found in a monograph.

Particularly noteworthy is the obvious impartiality of the editor in presenting more than one viewpoint on certain controversial subjects. For instance, Richmond C. Holcomb's study of the Haitian history of the origin of syphilis, which he calls a "fatuous but romantic tradition," presents the thesis that syphilis is a disease of prehistoric origin with pre-Columbian existence in Europe, Asia, Polynesia and other places; this is immediately followed by William A. Pusey's "Case for the American Origin of Syphilis." Furthermore, Charles S. Butler's thesis asserts that syphilis and yaws are the same disease, while that of Howard Fox contends that they are different diseases. Ellis Herndon Hudson's fascinating story of Bejel is an important inclusion. Five different articles on the biology of *Treponema pallidum* by Ingraham, Olsen, Turner, Pearce and Beerman present a concentrated but fairly comprehensive story of the organism.

Immunity, pathology, various clinical studies, serology, chemotherapy, pharmacology and public-health aspects are presented by such an array of authorities as Michelson, Kahn, Kline, Kolmer, Solomon, Tatum, Wile and Parran, as well as others. This monograph should be on the "must list" of every syphilologist, and on the shelf of every library.

The New England Journal of Medicine

Copyright 1940 by the Massachusetts Medical Society

VOLUME 223

OCTOBER 10, 1940

NUMBER 15

WEIL'S DISEASE IN THE UNITED STATES*

Report of a Case in Connecticut

FRANCIS G. BLAKE, M.D.†

NEW HAVEN, CONNECTICUT

IN 1935, Jeghers, Houghton and Foley¹ reported the first established case of Weil's disease from New England, reviewed the literature concerning leptospirosis and summarized the data concerning 11 previous sporadic cases that had been reported from various parts of the United States, including 4 from New York,²⁻⁴ 1 from New Jersey,⁵ 2 from Pennsylvania,⁶ 1 from the District of Columbia,⁷ 1 from Virginia⁸ and 2 from California.⁹ In all but 2 of the reported cases the correctness of the clinical diagnosis appears to have been well supported by the successful transmission of leptospiral infection to guinea pigs with blood (4 cases), urine (3 cases), spinal fluid (1 case) or kidney tissue (1 case), or by the satisfactory microscopic demonstration of leptospirae in tissues obtained at autopsy (3 cases). In 1 case⁸ confirmation of the diagnosis was based solely on the demonstration of "a few typical parasites" in dark field examination of the blood on the tenth day of the disease, while in 1 case,⁹ concerning which there may be some doubt, occasional spiral forms, which were described as appearing more like spirilla than leptospirae, were seen in sections of the kidney stained by Levaditi's method.

Since 1935, sporadic cases have been recorded with increasing frequency. In 5 of these, from Virginia,¹⁰ Michigan,¹¹ New York,^{12, 13} and New Jersey,¹⁴ the diagnosis seems to have been adequately supported by confirmatory laboratory tests, namely, successful transmission of the infection to guinea pigs in 4 cases, with additional demonstration of *Leptospira icterohaemorrhagiae* at autopsy in 2, and the development of specific agglutinins to a titer of 1:30,000 in 2. In addition to these 5 fully documented cases, 11, all from California, are incidentally referred to by Meyer,

Stewart-Anderson and Eddie,¹⁵ and 1 from Rochester, New York,¹⁶ is cited by Syverton, Stiles and Berry.¹⁷ Seven cases have been reported from Colorado,¹⁷ but the apparent ease with which numerous leptospirae were supposedly seen in dark-field examinations of the blood for long periods of time is so inconsistent with usual experience as to cast doubt on the validity of the diagnoses. Concerning the remaining 7 cases reported, 3 from Texas¹⁸ and 4 from Rhode Island,¹⁹ the data presented are so limited that evaluation is difficult.

The case reported here appears to be the first recorded from Connecticut.

CASE REPORT

A 29-year-old dairyman, of Wallingford, Connecticut, previously well, was suddenly seized on the afternoon of November 11, 1939, with pain in the calves of both legs, weakness and dizziness. During the evening he became progressively sicker, with chills, fever and headache. About midnight his neck became stiff and painful. He was severely nauseated and vomited frequently. He was seen by his physician, Dr. Charles A. Breck, early on the morning of November 12 and was referred to the Meriden Hospital.

At physical examination on admission the patient appeared acutely ill, bathed in perspiration, pale, weak and apprehensive. The conjunctivae were injected, the lips were dry, and the tongue was dry and coated. The neck was slightly stiff and painful. The lungs showed a few moist rales at the left base posteriorly. The blood pressure was 96/68. There was slight tenderness of the abdominal muscles. The liver and spleen were not felt. All deep reflexes were slightly hyperactive. The abdominal reflexes were lacking, the Kernig test was negative. The temperature was 102.6°F, the pulse 90 and the respirations 20. There were no other abnormal findings.

The white-cell count was 27,350, with 96 per cent polymorphonuclear neutrophils (nonfilament, 57 per cent, filament, 39 per cent) and 4 per cent lymphocytes. The urine was amber-colored, slightly cloudy and acid, with a specific gravity of 1.014. It showed no albumin or

*From the Department of Internal Medicine, Yale University School of Medicine and the Medical Service, New Haven Hospital, New Haven, Connecticut.

†Serving Professor of Medicine, Yale University School of Medicine and physician in chief, New Haven Hospital.

In addition to the other cases not yet reported here occurred in Rochester, New York (Breck, G. P. personal communication).

It is indebted to Drs. T. L. Murdock and J. A. Wilson of Meriden and Dr. C. A. Breck of Wallingford for making available the clinical record of this case prior to admission to the New Haven Hospital.

sugar. The sediment contained numerous epithelial cells. A Kline test was negative. The nonprotein nitrogen of the blood was 36 mg. per 100 cc., and the blood sugar 107 mg. X-ray examination of the chest was negative. A lumbar puncture showed an initial pressure of approximately 250 mm. of water. Ten cubic centimeters of clear spinal fluid was withdrawn; the fluid had a cell count of 30 per cubic millimeter, mostly red blood cells; a Pandy test was negative; a stained smear contained no organisms and rare lymphocytes; a culture showed no growth. Blood cultures showed no growth. Agglutination tests for typhoid and paratyphoid fevers and brucellosis were negative.

The subsequent course of the illness is shown in Figure 1. The predominant symptoms during the first 4

vision seemed slightly blurred, and he vomited on two occasions. On December 12, the 27th day of his illness, he was admitted to the New Haven Hospital for further study. Except for an elevated temperature, slight stiffness of the neck, a palpable liver extending 1.0 cm. below the right costal margin and some muscular soreness on flexion of the legs, the physical examination revealed nothing abnormal. The results of laboratory and other special examinations and the subsequent course of the illness are shown in Figure 2. The patient was discharged improved on December 18.

A few days after admission, review of the clinical course of the illness clearly suggested Weil's disease. The patient stated that about 10 days before the onset of his disease he had been engaged in tearing down an old barn

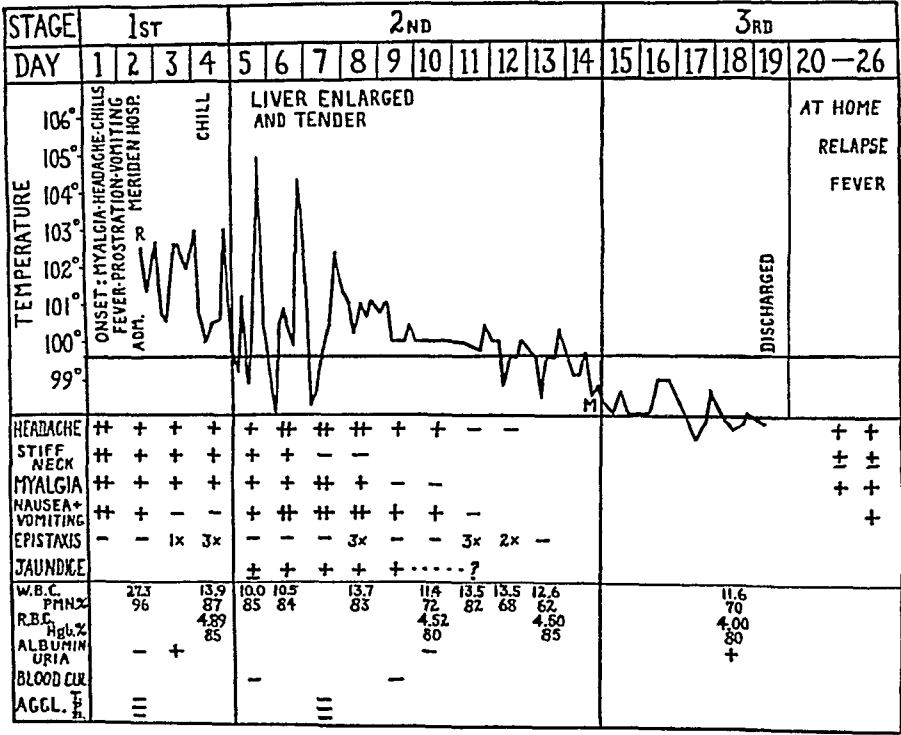


FIGURE 1. Early Clinical Course of Patient with Weil's Disease at the Meriden Hospital. Agglutinins: T—typhoid bacilli; P—paratyphoid A and B bacilli; B—brucella organisms.

days were prostration, fever, headache, meningismus and severe myalgia, principally in the neck, back and legs. On the 3rd day epistaxes began, recurring at intervals until the 13th day. A second lumbar puncture on the 4th day revealed a clear spinal fluid under normal pressure with 80 red blood cells per cubic millimeter. On the 5th day moderate jaundice developed; it lasted about a week. The liver became palpable and tender. The spleen was not palpable. With the jaundice there were severe nausea and vomiting, the vomitus on the 7th and 8th days containing blood. Evidence of renal involvement was negligible. From the 10th day on the patient steadily improved, the temperature reaching normal by the end of the 2nd week. He was discharged on the 19th day for further convalescence at home, no diagnosis having been established.

After returning home the patient again developed moderate headache and soreness in the legs. His appetite was poor, and he felt drowsy and somewhat feverish. His

which was swarming with rats. Dark-field examination of the urinary sediment on the 33rd and 34th days of the disease, possibly too late for a positive result, failed to reveal leptospirae, but samples of blood serum collected on the 38th and 47th days and submitted to the National Institute of Health in Washington, D. C., were reported to show complete agglutination with Type 1 *L. icterohaemorrhagiae* to a dilution of 1:10,000 and 1:30,000, respectively. Positive agglutination at these titers is considered diagnostic of leptospiral infection.²⁰ Taken in conjunction with the history of exposure to rats, an appropriate incubation period and the typical course of the illness with its three characteristic stages, the positive agglutination tests, with a rising titer between the 38th and 47th days, seem adequate to establish the diagnosis of Weil's disease.

The exact incidence of Weil's disease in the United States is uncertain, although the increas-

ing frequency with which cases are recognized suggests that it may be more prevalent than is generally supposed. That there is a large reservoir of *L. icterohaemorrhagiae* in the rat population has been well established through numerous surveys.^{15 16 21} It is likewise well established that the carrier rat which contaminates its environment by excreting leptospirae in its urine is the usual source of infection for man. Under these circumstances it is not surprising that the well authenticated cases that have been reported in this

which is not found in rats, and which, unlike *L. icterohaemorrhagiae*, possesses but little virulence for guinea pigs.²² That man may be infected with *L. canicola*, as well as with *L. icterohaemorrhagiae*, is now well established, particularly through the studies of Schuffner²⁰ in Holland, where human canicola fever has been shown to occur. It seems not improbable that the same is true of this country, for Meyer, Eddie and Stewart-Anderson^{15 22} have already demonstrated that canine leptospirosis is prevalent in California, and have cited a case of

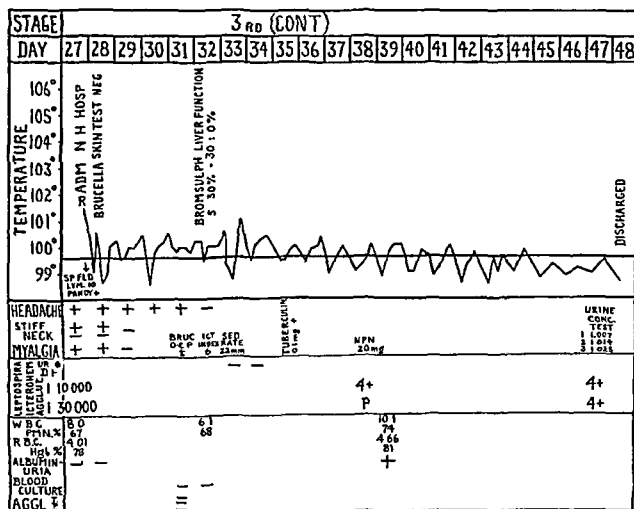


FIGURE 2 Further Clinical Course at the New Haven Hospital
D+ — dark field examination OCP — opsonocytaphag index

country have all been sporadic, and with 3 exceptions have occurred in men, many of whom were known to have lived or worked in places infested with rats. Of the exceptions 1 patient was a woman accidentally infected in the laboratory,² 1 young child stated to have contracted the infection from a pet dog sick with leptospirosis¹² and 1 schoolboy living in a rat-infested shack and engaged for several months in trapping rats.¹¹

The susceptibility of dogs to infection with *L. icterohaemorrhagiae* through contact with rats and the possibility that the dog may on occasion act as an intermediate vector between rat and man have received considerable attention,^{20 22 23} and are illustrated by the case reported by Martner.¹¹ This series of events should not, however, be confused with true canine leptospirosis,²⁴ a disease of older dogs caused by *L. canicola*, an organism

human infection with *L. canicola* in a veterinarian's assistant at Stockton.

A clinical diagnosis of Weil's disease may doubtless be readily suspected in an otherwise obscure infection after the onset of the second stage of the disease with jaundice, hemorrhage and evidence of renal damage, particularly if the patient is a sewer worker,²⁵ fish handler,²⁶ slaughterhouse worker or miner, or is known to live or work in rat infested premises or to have fallen into polluted water.²⁰ Overemphasis on the symptomatology of the second stage of the disease, however, especially the icteric and hemorrhagic features, which in many cases may be quite minor or even lacking,²⁰ should yield place to a greater emphasis on the characteristics of the first stage, if earlier diagnosis and more frequent recognition of Weil's disease are to be accomplished. These character-

istics are well illustrated by the case reported here, namely, abrupt onset with severe myalgia, particularly in the calves but also in other muscles, promptly followed by chills, fever, headache, nausea and vomiting, and suggestive symptoms and signs of meningeal irritation. Conjunctival injection is often a conspicuous feature. Herpes and hiccoughing may be present. Further than this, physical examination will add little. There will be a polymorphonuclear leukocytosis, with an increase in the proportion of immature cells. Other ordinary laboratory examinations are of little value in differential diagnosis.

While the foregoing group of symptoms is common at the onset of many severe acute infections, their persistence for two or three days without the development of further evidence of some well-recognized infectious disease might well lead to a suspicion of Weil's disease. Questioning a possible source of infection and a search for leptospirae in the blood and spinal fluid by dark-field examination, culture and guinea-pig inoculation, at a time when they are still present and most readily recoverable, would then be indicated. Subsequent confirmation of the diagnosis in a suspected case may be sought by dark-field examination and guinea-pig inoculation of the centrifuged sediment from 50 cc. of freshly passed urine* from the sixth to the thirtieth day of the disease, and by serum agglutinin tests after the tenth day. Biopsy of the gastrocnemius muscle may be of value. Vacuolation, swelling, loss of striations and hyalinization of isolated or groups of adjacent muscle fibers and infiltration with histiocytes, polymorphonuclear leukocytes and plasma cells may be seen on microscopic examination.¹ Of the laboratory procedures available, animal inoculation, blood cultures and serological tests appear to be the most reliable, and dark-field examination of the blood and urine the least satisfactory and most difficult.²¹ The agglutination test requires experience. For this reason, samples of serum should be submitted to a laboratory thoroughly familiar with the technic, such as the National Institute of Health.

It has often been suggested that epidemic infectious jaundice, outbreaks of which occur with considerable frequency in this country, may be of leptospiral etiology and represent a relatively mild, epidemic form of Weil's disease. No evidence substantiating this view, however, had been adduced up to 1923,²⁷ nor have more recent efforts^{28, 29} to isolate leptospirae from patients with epidemic jaundice been successful. Although Slesinger and

Zeligman²⁹ recorded that the National Institute of Health had reported positive agglutination reactions against *L. icterohaemorrhagiae*, with several specimens of convalescent blood from both jaundiced and non-jaundiced cases in the epidemic studied by them in Windber, Pennsylvania, it is their opinion that the cases were the usual type of epidemic infectious jaundice and not Weil's disease.³⁰

Up to the present at least, the epidemiologic and certain of the clinical characteristics of Weil's disease, as it has occurred in this country, have been quite distinct from those of epidemic infectious jaundice. The former has been recognized only as a sporadic disease occurring almost solely in adult men, while the latter commonly occurs in familial, institutional and community epidemics and largely among children, adolescents and young adults of both sexes.²⁷ The severe symptoms of the hemorrhagic and renal phenomena of the second stage of Weil's disease are, at most, quite rare in epidemic infectious jaundice. The polymorphonuclear leukocytosis of Weil's disease is also usually lacking in epidemic jaundice, which commonly exhibits a normal or somewhat low white-cell count, not infrequently with a relative lymphocytosis. In view of these contrasts it would seem appropriate to regard the two diseases as distinct until the etiology of epidemic infectious jaundice has been determined. Sporadic cases of so-called catarrhal jaundice, which clinically closely resemble individual cases of epidemic infectious jaundice, might perhaps be regarded with more suspicion as possible cases of mild leptospirosis, but here again evidence is wanting and further study is needed.

How often the more frequent consideration of Weil's disease as a possible diagnosis and the application of appropriate diagnostic procedures will prove fruitful is, of course, impossible to predict. At least they may serve to determine whether sporadic cases of leptospirosis are as prevalent in this country as they appear to be in Great Britain^{25, 26} and elsewhere in Europe.²⁰

SUMMARY

A case of Weil's disease in Connecticut is reported. The occurrence of the disease in the United States is briefly reviewed. The more frequent recognition and diagnosis of Weil's disease would appear to depend on a wider appreciation of its prevalence, a greater familiarity with its clinical symptomatology, particularly that of the initial pre-icteric stage, and a more frequent use of laboratory tests of proved diagnostic value at appropriate stages of the infection.

*Centrifugation is practically useless unless an angle centrifuge and high speeds are used. It is essential that the urine have an alkaline or at least a neutral reaction (Berry, G. P.: personal communication).

Since the preparation of this report 7 additional cases in or near Detroit, Michigan, have been recorded.³¹ Four of these occurred in men and 3 in persons in their teens, 1 of whom was a girl of fourteen. Three of the adults were poultry dressers.

789 Howard Avenue

REFERENCES

- Jeghers H J, Houghton, J D, and Foley J A. Weil's disease report of a case with postmortem observations and review of recent literature. *Arch Path* 20: 447-476 1935
- Wadsworth, A., Langworthy H V, Stewart F C, Moore A C, and Coleman M B. Infectious jaundice occurring in New York State: preliminary report on an investigation with report of a case of accidental infection of the human subject with *Leptospira icterohaemorrhagiae* from the rat. *J A M A* 78: 1120 1923
- McDowell E S. Infectious jaundice. *New York State J Med* 25: 19 1925
- Cushing E H. Leptospirosis icterohaemorrhagica. *J A M A* 89: 1041-1043 1927
- Saifer J. Leptospirosis icterohaemorrhagica (Weil's disease). *Am J M Sc* 170: 332-341, 1925
- Hyman J M, Jr., and Lynch F B Jr. Spirochetal jaundice in the United States. *Am J M Sc* 173: 80-89 1927
- Towler, H H., and Walker J E. Spirochetal jaundice: report of a case. *J A M A* 89: 86-89 1927
- Mulholland, H B., and Bray W E. Spirochetal jaundice: a case in Virginia. *J A M A* 90: 1113, 1928
- Bull H A. Leptospirosis jaundice: report of two cases. *Am J Clin Path* 3: 283-290, 1933
- Mulholland H B., and Bray, W E. Weil's disease: report of a case with autopsy findings. *Internat Clin* 4: 122-125 1937
- Martner, E E. Weil's disease: report of a case occurring in a child. *J Pediatr* 14: 48-50 1939
- Gloyer S. Weil's disease: report of a case in a fish worker. *J A M A* 110: 2143-2145, 1938
- Elton N W. Spirochetal jaundice in Buffalo, New York: report of a fatal case in a fish merchant. *Am J Clin Path* 9: 219-225 1939
- Hasche, W., and Tobey P J. A case of Weil's disease. *J A M A* 113: 1319-1321, 1939
- Meyer, K F., Stewart Anderson B., and Eddie, B. Epidemiology of leptospirosis. *Am J Pub Health* 29: 347-353, 1939
- Syvertsen J T, Stiles, W. W., and Berry, G P. Epidemiological studies on Weil's disease with notes on the susceptibility of the "gopher," *Citellus richardsoni* (Sabine), to the experimental inoculation of *Leptospira icterohaemorrhagiae*. *J Bact* 36: 279, 1938
- Gaines, A R., and Johnson R P. Weil's disease: report of seven cases. *Arch Int Med* 60: 817-836 1937
- Little O W. Spirochetal icterohaemorrhagica: report of three cases. *Texas State J Med* 32: 305 1936
- Liskey H G. Spirochetal icterohaemorrhagica. *Rhode Island M J* 22: 135, 1939
- Schiffner W A P. Recent work on leptospirosis. *Tr Roy Soc Trop Med & Hyg* 28: 7-37, 1934
- Noguchi, H. *Spirochaeta icterohaemorrhagiae* in American wild rats and its relation to the Japanese and European strains. *J Exper Med* 25: 555-763 1917
- Jobling, J W., and Eggstein, A A. The wild rats of the southern states as carriers of *Spirochaeta icterohaemorrhagiae*. *J A M A* 69: 1787, 1917
- Otteaen, A. The spirochete of infectious jaundice (*Spirochaeta icterohaemorrhagiae*, *Isaia* leptospira Noguchi) in house rats in Chicago. *J Infect Dis* 24: 485-488 1919
- Meyer, K F., Eddie B., and Stewart Anderson B. Canine murine, and human leptospirosis in California. *Proc Soc Exper Biol & Med* 38: 17-19 1938
- Molner, J G., and Kaiser J A. An outbreak of jaundice in Detroit: preliminary report. *J A M A* 110: 2069 1933
- Topley, W C., and Wilson G S. *The Principles of Bacteriology and Immunology*. Second edition. 1961 pp. Baltimore: William Wood & Co., 1916. Pp. 1445-1450
- Fairley, N H. Weil's disease among sewer workers in London. *Brit M J* 2: 10-14 1934
- Davidson, L S P., and Smith J. Weil's disease in fish workers: a clinical, chemical and bacteriological study of forty cases. *Quart J Med* N S 5: 263-286 1936
- Blumer G. Infectious jaundice in the United States. *J A M A* 81: 353-358 1923
- Willitt J C., Sigoloff, E., and Pfau C L. An institutional outbreak of epidemic jaundice. *J A M A* 106: 1644-1646 1936
- Slesinger, H A., and Zeigman, I. Acute infectious duodenitis (infectious jaundice): report of seventy-six cases. *J Pediatr* 14: 213-219, 1939
- Slesinger, H A. personal communication
- Molner, J G., and Meyer K F. Jaundice in Detroit. *Am J Pub Health* 30: 509-515 1940

ADVANCES IN THE ROENTGEN-RAY TREATMENT OF TUMORS OF THE BLADDER*

FLETCHER H. COLBY, M.D.,† AND RICHARD DRESSER, M.D.‡

BOSTON

IN THE spring of 1937, a roentgen-ray therapy unit operating at from 1000 to 1200 kv., constant potential, was put in operation at the Collis P Huntington Memorial Hospital in Boston. This apparatus has since been used chiefly for the treatment of deep-seated malignancies. The routine setting for such treatment is 70-cm. distance and a filter of 3.5 mm. of lead plus 8 mm. of copper. When a gold anode is employed, the output is 80 r per minute per milliamper of current. The average wave length of the radiation obtained is essentially that derived from a radium applicator filtered with the equivalent of 2 mm. of lead. The quantity of radiation is equal to that which might be obtained from about 2000 gm. of radium.

The advantages of this type of radiation are fourfold. Because of the high intensity it becomes feasible to use a long target-to-skin distance, there-

by increasing the depth dose. Approximately 50 per cent of the radiation delivered at the surface reaches the center of the average-sized pelvis. There is a greater tolerance of the skin as compared with the usual 200-kv. rays. This has not only been observed in human beings but has been demonstrated experimentally in animals. The amount of radiation reaching deeply is very little affected by the size of the portal of entry. It is therefore possible to use smaller fields covering only the disease-bearing area without having to resort to large portals to increase the depth dose. With small portals of entry, the amount of scattered radiation is about one third of that produced at 200 kv. This results in a lessened general reaction (roentgen sickness) on the part of the patient.

The skin reaction is generally the limiting factor in the treatment of deep-seated neoplasms with 200-kv. rays. The reverse, however, is true with supervoltage radiation. There is no longer a question of damage to the superficial structures,

*From the Collis P Huntington Memorial Hospital

†Assistant in surgery, Harvard Medical School, urologist, Collis P. Huntington Memorial Hospital

‡Instructor in roentgenology, Harvard Medical School, roentgenologist, Collis P. Huntington Memorial Hospital.

but the dosage is limited by the tolerance of the deep tissues, such as the intestines, bladder and so forth.

In view of the fact that radiation damage may not become manifest until several years after treatment has been concluded, it has seemed to us advisable to proceed with caution. A routine preliminary series of treatments for carcinoma of the bladder, consisting of 200 r delivered to each of three pelvic portals, 12 by 12 cm., one front and two posterior oblique, has been established. This is frequently augmented by 600 r to each of two lateral portals. Treatment is administered at the rate of 400 r per day. During the third week most patients experience diarrhea with increased vesical irritation. There is remarkably little roentgen sickness, and other than the bladder and bowel complaints, most patients experience little reaction. A month after the treatment has been concluded the patients are cystoscoped, and if the tumor has regressed, further radiation is instituted. The amount of radiation given in the second series is dependent on the general condition of the patient and the response of the tumor. We have not yet determined the maximum dosage which it is safe to give. We have been impressed with the dearth of untoward reactions in normal structures, and it seems likely that doses much greater than we have thus far employed will eventually be considered justifiable. As one of us (R.D.¹) has pointed out in an earlier communication, the amount of radiation administered in the preliminary series is not sufficiently large to ensure permanent control of carcinoma of the bladder.

Thirty-five patients with tumors of the bladder have been treated during the last three years at this clinic with the 1000-kv. roentgen-ray unit. Although the number of cases is small, these patients have been carefully studied and biopsies of the tumors have been taken before treatment in practically every case. Additional tissue has been removed from the tumors during and after treatment insofar as possible. Frequent cystoscopic examinations have served as an aid in determining radio-sensitivity and regression or disappearance of these new growths. The general condition of the patients and their ability to tolerate large amounts of external radiation have been determined by frequent physical examinations, blood counts and a follow-up routine.

We believe that supervoltage radiation differs sufficiently from other methods of treating tumors of the bladder to require a separate evaluation. Results so far seem to warrant its continuation, although supervoltage radiation is still in the ex-

perimental stage and its end results probably cannot be fairly evaluated for several years. Its value, we believe, should be considered at present not so much a means of curing cancer of the bladder as an agent which causes regression of the tumor and alleviates symptoms. With this point of view, so recent and untried an agent may be fairly evaluated.

As stated elsewhere, we² believe that localized tumors of the bladder are best treated by radical removal through excision, or destruction and implantation of radium. Supervoltage radiation has been used only to treat patients with extensive malignant tumors, unsuited to surgery, or those too feeble to stand operation. The patients included in this report, therefore, are chiefly debilitated individuals with advanced inoperable cancer. They have averaged sixty-two years of age.

Before starting supervoltage treatments tumor tissue has been obtained by biopsy or at operation in every case but 1. The exception was a huge

TABLE 1. *Classification of Tumors of the Bladder.*

TYPE	NO. OF CASES	PER CENT
Papillary carcinoma, Grade I	3	9
Papillary and infiltrating carcinoma, Grade II <i>a</i>	17	49
Infiltrating carcinoma, Grade II <i>b</i>	6	17
Nonpapillary infiltrating carcinoma, Grade III	6	17
Sarcoma	1	3
Ungraded	2	6
Total	35	

infiltrating tumor of the bladder, obviously malignant. These tumors were classified according to the Tumor Registry of the American Urological Association* as shown in Table 1.

The papillary infiltrating type of growth was the commonest in this series, although nonpapillary infiltrating tumors comprised about one third of the cases.

Biopsies have been a valuable aid, although disappointing in some respects. In several cases of obviously malignant neoplasms the report from the first biopsy was "chronic inflammation." On the other hand, tissue removed from areas grossly but not frankly neoplastic sometimes contained actively growing tumor cells. This was particularly

*The official basis of grading is as follows

Grade I. Papillary carcinoma: all papillary tumors in which there is no clinical evidence of infiltration, and in which no obvious infiltration of the pedicle or bladder wall can be demonstrated on histopathological examination, most of the cells are typical in appearance or arrangement.

Grade II. *a* Papillary and infiltrating carcinoma: obviously infiltrating papillary tumors and carcinomas in which the papillary structure is recognizable but most of the cells are atypical in appearance and arrangement. *b* Infiltrating carcinoma: nonpapillary squamous cell carcinomas in which the cells are fairly uniform in size and type or have a tendency to form keratohyline and epithelial pearls.

Grade III. Nonpapillary infiltrating carcinoma: very anaplastic, infiltrating carcinomas, practically all the cells atypical in appearance, very slight or no differentiation.

true among patients whose tumors disappeared as a result of radiation, and here a positive biopsy report demonstrated the need for further treatment. Biopsy, however, proved disappointing as an indication of the radio-sensitivity of tumors, although further study of the correlation of histology and radio-sensitivity would be helpful. Biopsy was useful in establishing a diagnosis of papillary carcinoma, Grade I, since such tumors responded slightly, if any, to external radiation. Our experience in this respect has paralleled that of tumors

gressed, sometimes to an astonishing degree, and over 60 per cent disappeared, at least for a time. Such tumors were likely to recur rapidly, however, and in none has there been evidence of prolonged permanent cure.

With tumors of moderate malignancy, the papillary and nonpapillary types of growth were about equally radio-sensitive. The chance that such tumors may respond favorably to this form of radiation appears to be good, since there was regression in over 60 per cent of our cases. Gross disappearance occurred in about one third of these growths. It is doubtful if any cases were cured by radiation alone, although in a few sufficient regression resulted to allow transurethral removal of the remaining tumor and radium implantation. Several cases so treated have remained free of tumor long enough so that the chances of cure are excellent.

Epithelial tumors of the lowest grade of malignancy, the benign papillary type, responded poorly to radiation. The 3 cases reported were huge tumors which filled most of the bladder cavity but histologically were papillomas. One such growth, composed of very delicate, long papillary projections, disappeared except for a few small nubbins which were easily, and probably permanently, destroyed by transurethral fulguration. No effect other than the control of bleeding was as a rule obtained in tumors of this type by supervolt-

TABLE 2. *Individual Dosage.*

PATIENT	AGE yr.	DOSAGE r.	PATIENT	AGE yr.	DOSAGE r.
T. B.	83	8,400	F. K.	60	8,400
F. S. B.	80	6,000	G. M.	58	20,800
W. B.	48	8,400	W. M. A.	47	13,200
Z. B.	57	13,900	P. M. C.	62	10,200
A. B. C.	63	14,900	J. M. E.	73	6,000
A. M. G.	77	12,800	J. M. K.	58	10,600
M. C.	69	12,000	J. N.	75	9,600
C. L. C.	74	17,300	C. P.	62	7,200
J. E. C.	63	6,000	C. A. P.	64	12,000
T. D.	58	6,400	A. S.	62	7,600
R. T. E.	82	12,000	A. S.	46	13,600
H. F.	74	22,200	A. S.	52	12,000
J. F.	73	10,000	M. S.	35	6,000
J. G.	34	4,200	S. T.	44	10,200
A. G.	68	12,400	G. T.	78	6,000
L. R. H.	59	12,400	I. T.	59	6,800
F. H.	77	7,700	N. V.	33	6,400
R. H.	73	7,200			

of other organs: the less differentiated the cell type, the more radio-sensitive the tumor. Except for this generalization, however, it has not been possible to gauge radio-sensitivity from the histological examination of biopsied specimens.

Table 2 shows the individual dosage given in this series of cases.

Our experience regarding the response of the different types of bladder neoplasm to radiation is summarized in Table 3. As a result of treatment, over half of these tumors regressed, that is, were reduced by at least one third. Gross disappearance, as determined by cystoscopic examination, occurred in about one third of the cases. Frequently, however, the disappearance was only temporary and recurrence was obvious in a few weeks or months. The effects of radiation seemed more marked on the intravesical portions of these tumors than on the parts that had deeply invaded the bladder wall. In many cases induration of the bladder wall persisted and was readily detected by rectal or vaginal examination. Biopsies were positive in a number of such cases, although, otherwise, frank tumor could not be identified.

The tumors most sensitive to radiation were the rapidly growing neoplasms with little or no cell differentiation, the infiltrating Grade III carcinomas. Over 80 per cent of such growths re-

TABLE 3. *Response of Types of Bladder Neoplasm to Radiation.*

TYPE OF TUMOR	NO. OF CASES	REGRESSION OF TUMOR		GROSS DISAPPEARANCE OF TUMOR	
		NO. OF CASES	PER CENT	NO. OF CASES	PER CENT
Grade I	3	1	33	0	0
Grade II a.	17	11	64	5	29
Grade II b.	6	4	66	3	50
Grade III	6	5	83	4	66
Sarcoma	1	0	0	0	0
Ungraded	2	0	0	0	0
Totals	35	21		12	
Average percentages			60		34

age treatment. External radiation may be useful even in this group, however, to stop persistent bleeding and to improve the patient's condition enough to stand open operation.

One case of sarcoma of the bladder was not benefited by external radiation. This tumor was either leiomyosarcoma or rhabdomyosarcoma.

Bleeding or frequent and painful urination was relieved in over half the cases. Such relief was frequently only temporary, and symptoms returned with extension or reappearance of the growth. An occasional patient was made worse by treatment.

CONCLUSIONS

Roentgen rays produced at 1000 kv., constant potential, afford a means of delivering to deep-seated neoplasms doses which are limited not by skin effect but by the tolerance of underlying structures. The results that we have obtained in radiating bladder tumors during the last three years with rays produced at this high potential are definitely superior to those we have observed in treating similar tumors with rays produced at lower voltages. Well-marked regression of the growth was obtained in about half the cases, with

at least temporary disappearance of the lesion in about a third. Pain and bleeding were relieved in approximately half the cases. It is our belief that as we gain experience with this type of radiation these results will improve.

Emphasis must be laid on the fact that this method is not a substitute for surgery. Tumors suitable for excision or resection should be handled by operation.

REFERENCES

1. Dresser, R., and Rude, J. C.: Supervoltage roentgen treatment of carcinoma of the bladder. *J. A. M. A.* 111:1834-1837, 1938.
2. Colby, F. H.: Supervoltage radiation in the treatment of bladder tumors. *Tr. Am. A. Genito-Urin. Surgeons* 31:227-244, 1938.

THE RIB JOINTS

JOEL E. GOLDTHWAIT, M.D.*

BOSTON

THERE are twenty-four joints, called the costovertebral joints, formed by the conjunction of the heads of the ribs with the sides of the spine. Besides these, there are twenty joints, called the costotransverse joints, formed by the angles of the ribs and the outer parts of the transverse processes of the upper ten dorsal vertebrae. This makes forty-four joints involved in the mechanism of the thorax, each being a true joint and capable of disease or injury as would be true with other joints, with the added disadvantage that while most of the others have periods of rest after periods of activity the rib joints, unless they become ankylosed from disease, never rest entirely so long as life exists.

The costovertebral joints of the upper ten dorsal vertebrae are so placed that part of the articulation is with the vertebra above and part with the vertebra below, overriding the intervertebral disk, the location of the joint being just in front of the articular process. The two lower ribs form their articulations with the sides of the vertebrae, the eleventh and twelfth, and do not override the intervertebral disks.

The costotransverse joints are usually placed with the articular surface on the anterior part of the transverse process, but at times the articulation is actually on the top of the process, with all possible variations between these two extremes. If the articulation is on the top of the process, the surface is at times horizontal, while at other times it is oblique. Sometimes the location of

this transverse joint varies in the same individual, with several of the vertebrae, usually in the middle section, having their articulation on the upper part of the transverse process, while the other ribs have it directly in front (Fig. 1).

Another important feature in the function of the rib joints is the length of the transverse processes. Sometimes they are very short, at other times long, and the difference that the length of the process makes on the leverage that the main part of the rib exerts on the costovertebral joint is obvious.

The range of motion in the rib joints is limited by the anatomic structure and by the muscles and ligaments, the extreme range of motion being enough to allow movement of the thorax in full respiration to yield between 7 and 12 cm. difference in chest circumference. To ensure the normal use of these joints, the neutral position, that is, one about midway between that resulting from full inspiration and that resulting from full expiration, should be maintained, and to obtain this the ribs should slope downward from the spine about 30° (Fig. 2).

As the body is often held, the chest sags and the head and shoulders are rounded forward so that the ribs hang below the normal low point of rib function (Fig. 3). This means that the muscles and ligaments are out of balance, and that strain continued for any length of time must result in weakness and joint irritation. The position of a rib when the chest is lowered depends to a considerable extent on the position of the costotransverse joint, since if the articulation is on the

*Consultant in orthopedic surgery, Massachusetts General Hospital.

top of the transverse process, sagging of the rib must either rotate the head out of its normal position or act as a fulcrum and pry it up above that position. Regardless of whether the costotransverse articulation is on the top of the transverse process or in front, as the rib sags this joint is used as a fulcrum and the rib is either twisted, thus rotating the head abnormally, or actually forced into a different position from the normal one (Fig. 4). With the rib joints, as with all

chest wall or around the body at the different levels, with nothing apparent in the chest examination, are easily explained by irritation of the intercostal nerves at the costovertebral joints.

The circulatory disturbances often seen in connection with the irritation of these joints may be explained when one realizes that at the side of the spine, adjacent to the costovertebral joint, there is not only the root of the nerve supplying sensory and motor control, but also a ganglion of the

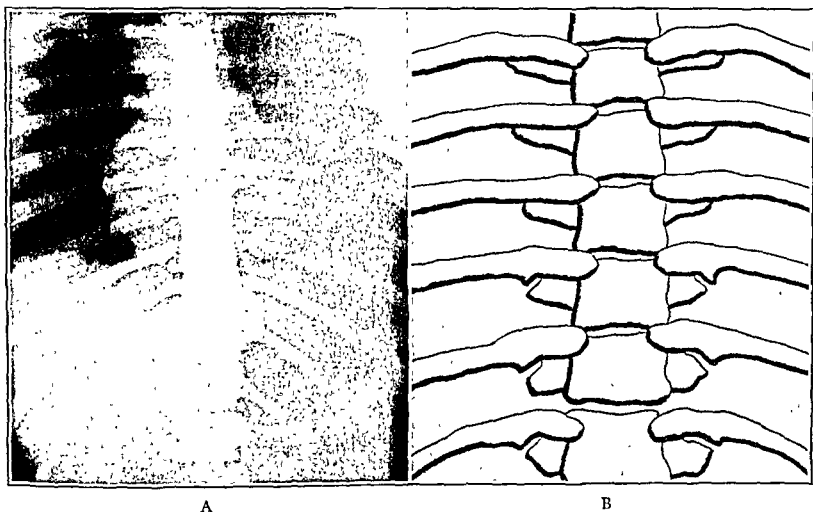


FIGURE 1.

A is a reproduction of an x-ray film showing the costotransverse joint of several of the lower ribs located on the top of the transverse process, while in the ribs above, the articulation is on the anterior part. B, a drawing made from this film, shows these joints more clearly.

others, if these faulty positions are long maintained irritation must result, with consequent changes in structure—true arthritic conditions (Fig. 5).

In such a condition, the symptoms resulting from the mechanical strain may be referred to the region of the costovertebral joints at the back, or along the sides of the chest, owing to the fact that at the level of each costovertebral joint a nerve trunk—the intercostal nerve—leaves the spine and passes along the rib, and irritation of the root of this nerve naturally refers symptoms to its distribution. Today very few of the cases of pain referred to the back of the leg, formerly called "sciatica," are treated with reference to the leg condition, but it is realized that most cases represent referred pain from conditions in the low back. So also, many cases of pain referred to the

sympathetic nervous system which is connected with the other cells of the system.

Commonly the disturbances in the rib joints are gradual in development and the symptoms are subacute or chronic. At times, as the result of definite wrench or injury, the irritation of the joint becomes much more marked and represents a true acute joint strain, with intense suffering and at times actual displacement of the head of the bone. In these cases the effect on the sympathetic ganglion is much more marked, and flushing of the face, with a change in the general superficial circulation, is likely to occur.

Once it is realized that these are true joints, subject to strain from overuse or violence exactly as with any other joint, it will be understood why they are liable to disease or injury like any other

joint. One of the common manifestations of disease is the atrophic type of arthritis (Fig. 5), which many times goes on to the complete ankylosis of these joints, so that no motion of the chest is made in respiration. When this stage has been reached, naturally the pain is largely overcome because there is no irritation of the joint as the result of motion.

Once this condition is recognized and the normal mechanics of the joint are understood, the

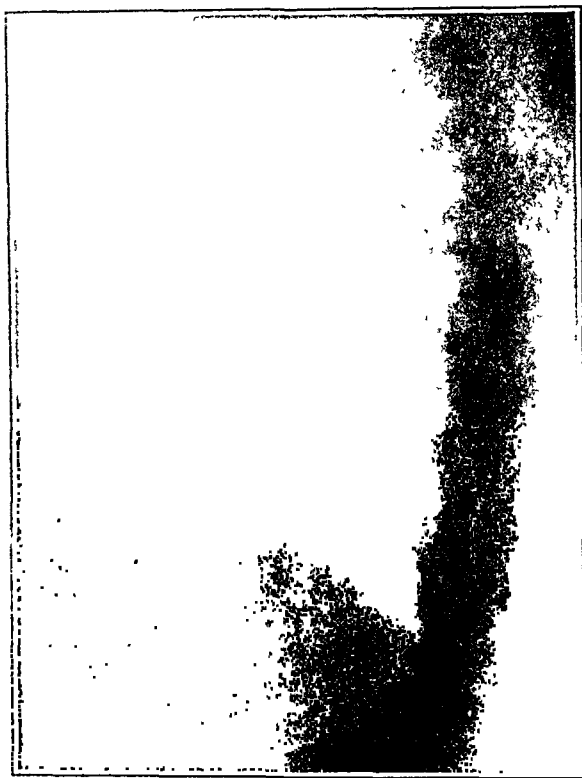


FIGURE 2.

This x-ray film shows a normal chest with the ribs in satisfactory position, the downward inclination below the horizontal being about 30°.

treatment naturally consists in having the body so held that the neutral position will be with the ribs midway between the position of full inspiration and that of full expiration. Often in order to obtain this effect, mechanical supports are needed until the joints have recovered from their irritation, or until the muscles have been so developed that the neutral, normal position is possible.

If there is extensive disease of the joints so that ankylosis becomes probable, it is also important that the ideal neutral position be obtained, since in this position the strain that must be placed on the diaphragm when the thoracic movement is

eliminated will be less than would be the case if the chest markedly sagged.

Since there is no costotransverse articulation to limit the motion of the main joint, and since the rib is not supported in front by the costosternal cartilage, the floating ribs, two on each side, are able to sag and move about much more, naturally with much greater strain on the rib joint, and with much greater possibility of irritation of the nerve root and trunks (Fig. 5). The posterior position that these ribs frequently assume must mean not only a marked backward position of the rib itself, with strain to the joint, but twist of the rib as well (Fig. 6). The referred pain that would come from irritation of

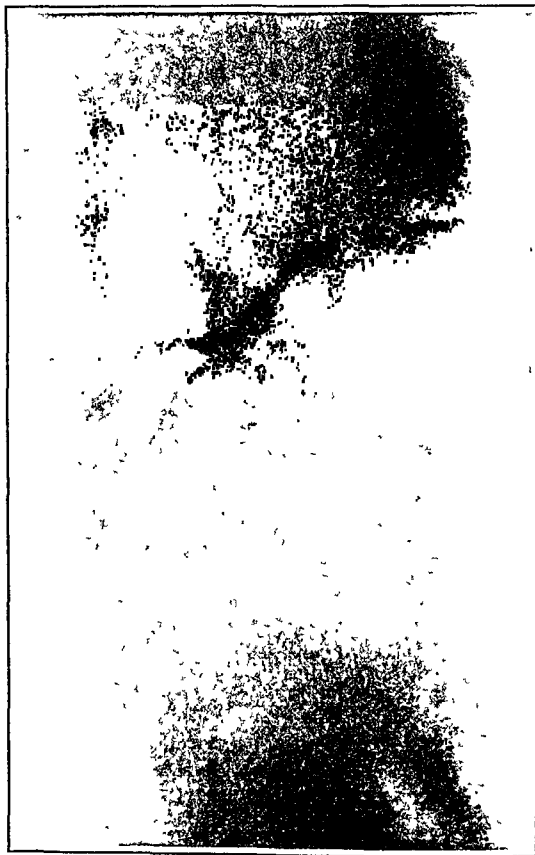


FIGURE 3.

This film demonstrates an extreme sag of the chest, with marked downward inclination of the ribs. The latter are considerably below the normal low position for respiration, and to obtain this position there must be a marked unnatural strain on both the costovertebral and the costotransverse rib joints.

the nerve roots adjacent to these ribs is referred to the sides of the abdomen from the pubic bone to the crest of the ilium, and it is this irritation that undoubtedly explains the so-called "abdominal pains" mentioned by Carnett.¹

CASE REPORTS

CASE 1 O R, a 19 year old boy, strong and healthy while working hard in some agricultural occupation had a sudden sharp pain referred to the right side extending down to the right side of the abdomen. The suffering was intense. When the patient was lying down palpation of the abdomen was almost impossible because of the extreme sensitiveness over the right side. At the same time

Comment The case undoubtedly represents one of acute sprain with twist or displacement of the head of the rib with resulting spasm of all the muscles related to that region, and with the pain referred to the distribution of the eleventh and twelfth intercostal nerves. Relief was obtained by placing the patient in a position in which the rib fell forward the correction of its twist being made by the mere sag of the body. No force was required to correct it. Recovery occurred rapidly with protection



FIGURE 4

This film shows not only a downward inclination of the ribs at the side but a distinct twist of the ribs so that the usual convex upward curve is convex downward. To obtain this position the heads of the bones must be pried upward and forward.

there was extreme sensitiveness over the joints of the eleventh and twelfth ribs on the right side. The patient's general condition was good and the blood count showed no evidence of a rapidly developing infection. As part of the examination the patient was put in the knee hand position getting up on his knees and hands and thus allowing the abdomen to sag, a few deep breaths were taken to relax the tension of the abdominal wall and to make it possible for the diaphragm to work freely as was impossible with the patient lying on his back. In a few minutes the pain was alleviated and the extreme sensitiveness over the costovertebral joints on the right side at the eleventh and twelfth ribs was entirely relieved. Palpation of the abdomen also became possible.

of the joints for a short time exactly as a sprain of any other joint would be treated.

CASE 2 B L, a 45 year-old woman, had had a great deal of difficulty referred to the abdomen over a period of years, for which six different abdominal operations were performed without relief of the pain. After much treatment the actual condition of irritation of the costovertebral joints was recognized proper treatment was given and the abdominal symptoms were entirely relieved.

Comment This case represents an arthritis of the costovertebral joints which had lasted for many years with irritation of the intercostal nerves. The condition was relieved by correcting the position of the ribs and allowing the irritation at the joints to clear. Some of the pain had

been referred to the anterior part of the ribs in the region of the liver, and the difficulty had been thought to be due to gall bladder disturbance.

CASE 3 L. G., a 60-year-old woman, had been in rather poor health and was beginning to develop an arthritis involving the spine and several of the other joints. The body had been held with moderate rounding of the upper dorsal spine, and exercises were planned as a part of the treatment to correct the curve of the dorsal spine and draw

has there been any other evidence of cardiac or vascular disturbance.

CASE 4. S. M., a 33-year-old woman, was seen because of pain referred to the upper part of the chest, chiefly on the left side, and extending somewhat into the left arm. The condition had been present for some time and had limited the patient's activities. Because 2 years previously she had had a small tumor, which was said to be benign, removed from the left breast, naturally she and her physi-

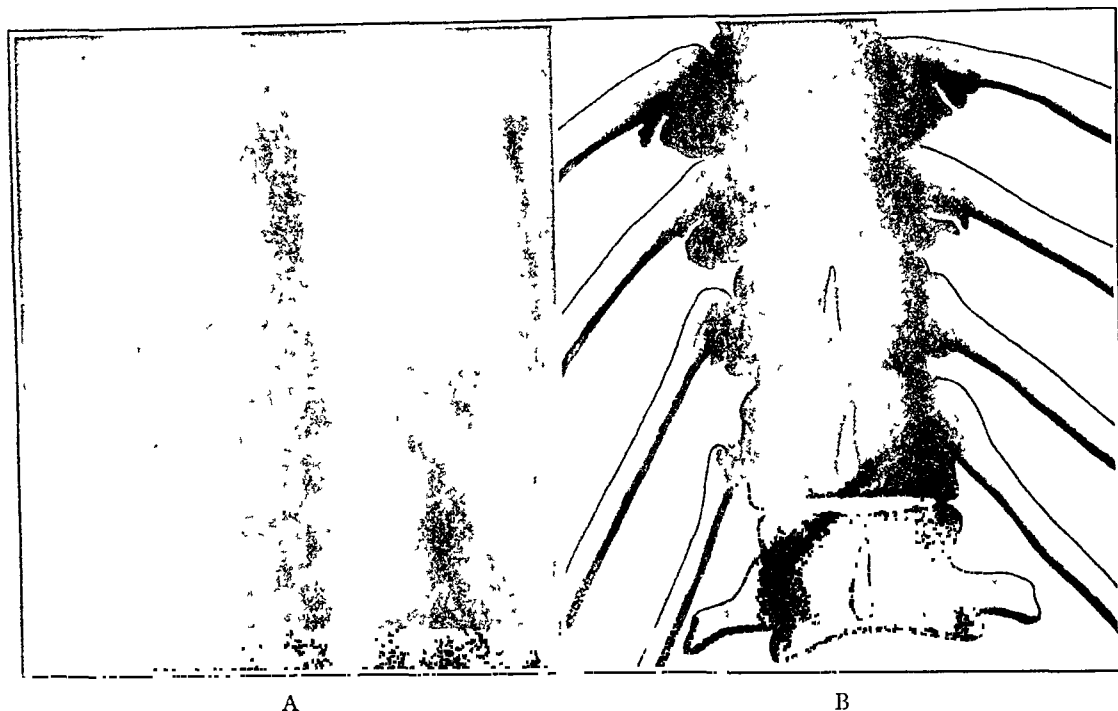


FIGURE 5.

A represents the x-ray film of a spine completely fused throughout the dorsal region from atrophic arthritis, with the rib joints also involved. The thickening about the costotransverse joint is very marked. Note also the downward inclination of the last ribs and the fact that on the right side the rib is practically in contact with the tip of the transverse process of the first lumbar vertebra, enough to cause pain from pressure on the intercostal nerve with reference along the side of the abdomen.

B, a sketch made from the film, shows the thickening about the rib joints. The complete fusion of the spine is indicated by the darkening of the whole spine, and the low position of the rib on the right side is clearly shown. The artist has made the vertebrae appear more dense than normal, while as a matter of fact the bones were much atrophied, with fusion of the intervertebral disks.

the ribs up into place. After taking some of the exercises the patient had sudden, acute pain referred to the left side of the chest, covering the distribution of the fifth and sixth intercostal nerves. The pain was so intense and the suffering was so great that the case was considered to be one of angina, with probable disturbance of the blood vessels of the heart. The patient was at once removed to the hospital by ambulance. Careful study was made of the heart with all the modern, approved methods, but no evidence of cardiac disease was found. In attempting to explain the symptoms, marked sensitiveness was noted over the costovertebral joints at about the fifth and sixth vertebrae. The acute symptoms were undoubtedly due to the fact that with the exercises given to improve the function of the upper dorsal spine some of the adhesions of the rib joints had been broken, with resultant acute irritation. Recovery from the acute strain was entirely normal, and the patient has had no further attacks, nor

can feared that the condition was a recurrence of that disease.

In the examination of the patient the body was held with the chest extremely low and quite flat in front, the dorsal spine rounded forward, the shoulders markedly sagged and the diaphragm naturally low. At the first examination there was marked tenderness over the costovertebral joints in the region of the fourth and fifth ribs, especially on the left side. The condition was recognized and the patient was admitted to the hospital, where the mechanical condition was overcome, with entire relief of the symptoms, a gradual lessening of the sensitiveness over the costovertebral joints and great mental relief to the patient.

These cases are used simply as suggestive or illustrative of disturbances at the different rib levels, but once one understands the rib-joint mechanism,

it becomes possible to realize that any of these forty four joints may become irritated, strained or diseased, with the added possibility of irritation of the nerves adjacent to the joints and pain referred to the distribution of the special nerves

SUMMARY

There are forty four true rib joints twelve costovertebral joints on each side where the ribs join

tween the extremes of inspiration and expiration Since there is a nerve which leaves the spine just at the level of each vertebra adjacent to the head of the rib, irritation of these nerves in connection with disease of the rib joint is easy to understand Also, since there is a sympathetic ganglion connected with the nerve adjacent to the head of the rib, some of the circulatory disturbances undoubtedly find their explanation in irritation of this ganglion

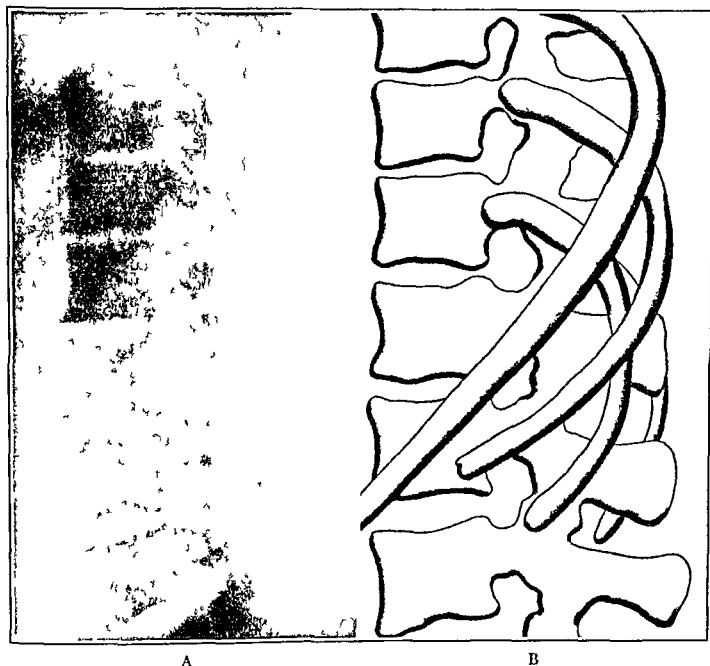


FIGURE 6

A is a lateral x-ray film showing the downward inclination of the lower ribs, with the marked posterior position commonly seen To obtain this position the rib joint must not only be strained but the rib more or less twisted

B is a drawing made from the film

the spine, and ten on each side of these where the ribs touch the tips of the transverse processes at their angles Each of these joints represents a true joint and is capable of disease or strain, as is any other joint Since the chest is constantly used in respiration, the fixation of the rib joints in connection with disease is more difficult than it is in other joints, and the best position for rest is one with the chest held in a position halfway be-

Once the anatomic and mechanistic condition is appreciated the treatment of disease of the rib joints should be fairly simple

372 Marlboro Street

REFERENCES

1. Carnett, J. B. Intercostal neuralgia as a cause of abdominal pain and tenderness. *Surg. Gynec. & Obst.* 47:625-632, 1927. Acute and recurrent neuralgia dependent on disease of intercostal neuralia. *Ann. J. M. Sc.* 174:813-851, 1921. The simulation of gall bladder disease by intercostal neuralgia of the abdominal wall. *Ann. Surg.* 86:47-52, 1927.

PRIMARY ECHINOCOCCAL CYST OF THE UTERUS*

MERRILL L. WELCKER, M.D.,† GEORGE D. KANE, M.D.,‡ AND RAYMOND H. GOODALE, M.D.§

WORCESTER, MASSACHUSETTS

CASE REPORT

ECHINOCOCCAL disease is rare in this country, and merits particular mention when it presents itself as a primary intrinsic tumor of the uterus. To our knowledge, the following case is the only one of its kind reported from North America.

Schatz¹ in 1885 collected 14 cases from the literature. Secheyron and Pean² nine years later

A 77-year-old, Albanian-born, married woman was admitted to the Genitourinary Service of the Worcester City Hospital on August 9, 1939, because of urinary retention and lower abdominal pain of 3 days' duration.

Physical examination revealed a well-developed, poorly nourished, woman in no acute distress. The lower abdomen presented a large, firm, slightly tender, immovable tumor in the midline. The liver, spleen and kidneys were



FIGURE 1. Echinococcal Cyst of Uterus.

The fibrous cyst cavity in the uterus is in the center of the photograph; the mother and daughter echinococcal cysts are seen at the sides.

added 4 cases. In 1918 Turenne³ and in 1920 Bull⁴ each described 1 case. Nurnberger⁵ in 1926 reviewed the literature and brought the count to 30, exclusive of the cases reported by Turenne and Bull. In the subsequent nine years, 9 more scattered cases were culled from the literature by Missirloglou and Anagnostidis,⁶ who added 1 case of their own, bringing the total to 42. We believe that ours represents the forty-third reported case of primary echinococcal cyst of the uterus.

*From the Department of Pathology, Worcester City Hospital, Worcester, Massachusetts.

†Pathology intern, Worcester City Hospital.

‡Graduate assistant, Medical Outpatient Department, Worcester City Hospital.

§Pathologist, Worcester City Hospital, assistant professor of experimental pathology, Boston University School of Medicine.

not palpably enlarged. Pelvic examination showed a small polypoid mass protruding from a marital introitus. The uterus, apparently the source of the tumor, extended 7.5 cm. above the symphysis pubis. It was firm, suggestively fluctuant and fixed. The adnexa were not remarkable.

The urine (catheter specimen) was acid and straw-colored, with a specific gravity of 1.016. It contained a slight trace of albumin, a few red and white blood cells, and squamous cells. The red-cell count was 3,750,000, the hemoglobin 70 per cent, and the white-cell count 9000 with 84 per cent polymorphonuclears, 14 per cent lymphocytes, 1 per cent large mononuclears, 1 per cent non-segmented cells and no eosinophils. The blood sugar was 110 mg. per 100 cc., and the nonprotein nitrogen 48 mg. Hinton and Kahn blood tests were negative.

During her hospital stay the patient's temperature vacillated between 96 and 100°F. Preparation for laparotomy was begun, but she rapidly developed symptoms of cardiac

failure and died on the ninth hospital day. At that time it was thought that she had either an adenocarcinoma or a fibroid of the uterus and that the protruding mass was a cervical polyp.

At autopsy the abdominal cavity contained no free liquid. The uterus measured 14 cm in diameter and filled the entire pelvis. It was symmetrical and presented a smooth pinkish-red surface. On section a cyst 13 cm in diameter was found in the posterolateral wall. The cyst was well circumscribed by a pearl-white mantle varying from 1 to

mainder of the protoplasm were many large vacuoles, of discrete nature and not forming any pattern.

A very few other forms of scolex were present, and from their slightly larger size and continuous activity were obviously more adult than those described above. They were pear shaped; the narrower portion of the pear being represented by the protruding head of the scolex, which remained in continuous motion and defied photography since it swayed from side to side and alternately protruded and retracted. The double ring of hooklets was situated at the stem of the pear, or at the most actively moving portion of the scolex (Fig 3). Almost complete retraction and reversion to the earlier quiescent form was accompanied by the introduction of a slight amount of formalin. The protoplasm coagulated and darkened, and then the violent movements ceased; the head protruding somewhat. No free hooklets were seen in any of the cyst fluid examined.

Echinococcosis of the uterus may be primary or secondary but is usually secondary. It is often the result of a generalized peritoneal seeding,

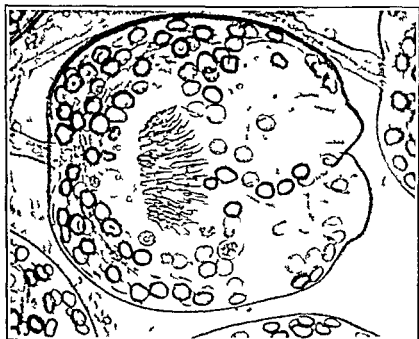


FIGURE 2 Scolex of *Echinococcus*

This was photographed alive unstained and non motile in the natural cyst fluid; the head is retracted. Note the double ring of hooklets in the center.

2 mm in thickness. One part of its surface presented small irregular granulations. It contained clear whitish fluid within which a few small whitish granules about 1 mm in diameter floated freely. Approximately a hundred smaller daughter cysts of various sizes, the largest of which measured 6 cm in diameter, were present in the uterus (Fig 1). These were all discrete and pearl white, were provided with thin translucent membranes and contained clear liquid and whitish granules similar to those in the parent cyst. No other abnormalities were encountered in the uterus except a polyp in the cervix. The tubes and ovaries were normal and not attached to the cyst. No cysts were found in the liver, kidneys, spleen or pleural or peritoneal cavities. A small amount of purulent material was found in both ureters and kidney pelves.

A few of the granules floating inside one of the larger daughter cysts were put on a glass slide, crushed and examined microscopically within 4 hours after death. Vast numbers of scoleces were seen. Most of them were discrete and almost round with a slight flattening of the cephalic end. Orientation of the scolex depended on the direction of the two rings of hooklets, which by virtue of their different refractility were clearly seen to be embedded deeply in the center of the organism. The cephalic flattening and the central nature of the hooklets were found to be results of retraction of the tip or active portion of the scolex, in which the rings of hooklets were inserted (Fig 2). These forms of scolex were evidently early and exhibited no movement until an addition of formalin to the medium brought forth several violent shudders culminated by a dark discoloration of the protoplasm and a failure of response to further stimuli. Scattered through the re-



FIGURE 3 Scolex of *Echinococcus*

This was photographed in the motile stage with the head protruding. The protoplasm is darkened by formalin which is used to eliminate motility for photographic purposes. Hooklets can be seen around the neck of the organism.

particularly in the posterior cul-de-sac. Primary infection most likely occurs directly via the vaginal canal. The primary cyst is comparatively voluminous, secondary cysts are smaller and multiple. The cyst varies in shape but is generally spherical, it is smooth and firm, and insidious, without functional disturbances. The cyst is painless and in most cases develops as a slowly expanding space-occupying tumor compressing neighboring organs—the bladder, rectum and ureter—and resulting in slight pain in the lower abdomen, becoming severer and radiating along the lower extremities. Exploratory punctures can not be condemned too strongly, for a variety of reasons. Skintography is of decided diagnostic value for echinococcosis of the lungs, liver and kidneys,

but is practically useless when the uterus is involved, because of the pelvic shadow. Biological methods such as skin tests have been utilized to reveal the presence of echinococcal disease. As shown in cattle by Goodale and Krischner,⁷ the skin test is more reliable than the complement-fixation test. The clinical outcome of echinococcosis of the genitals is the same as that when other organs are involved, namely, spontaneous cure, suppuration, discharge into some neighboring organ or death from hydatid cachexia. The first is exceptional. Primary echinococcal disease of the uterus may be first discovered at autopsy, as in this case. Secondary manifestations of pressure may be very dramatic and even cause death. If and when diagnosed, primary echinococcosis of the uterus should lend itself very favorably to surgery.

SUMMARY AND CONCLUSIONS

Forty-two cases of primary echinococcal disease of the uterus have been described in the literature. Our case is the forty-third and is, to our knowledge, the first to be reported from North America.

Its diagnosis, clinical course and treatment are briefly discussed.

REFERENCES

1. Schatz cited by Missirloglou and Anagnostidis.⁸
2. Secheyron and Pean: cited by Missirloglou and Anagnostidis.⁸
3. Turenne, A. Primary hydatid cysts of the uterus. *Surg., Gynec & Obst.* 26:446-449, 1918
4. Bull, L. J.: A case of hydatid cyst of the uterus. *St. Bartholomew's Hosp. J.* 25:82, 1920
5. Nurnberger, cited by Missirloglou and Anagnostidis.⁸
6. Missirloglou, A., and Anagnostidis, N.: Ein Fall vom primärem Echinococcus des Uterus. *Zentralbl. f. Gynäk.* 61:1297-1299, 1937.
7. Goodale, R. H., and Krischner, H.: Biological tests for hydatid disease: comparison of Casoni and Weinberg tests. *Am. J. Trop. Med.* 10:71-76, 1930

MENTAL PROBLEMS OF MID-LIFE*

A Review of 100 Cases

CURTIS T. PROUT, M.D.,† AND ALBERT U. BOURCIER, M.D.‡

ARLINGTON HEIGHTS, MASSACHUSETTS

DURING the past decade, a great deal of attention has been focused on mental illness occurring in the younger age group. Mental hygiene, with its child-guidance clinics, has devoted much effort to early attack on, and prevention of, mental disorders. During the same period, the much publicized "shock therapies" have practically monopolized the center of the psychiatric stage. More recently, as hospital statistics have shown a rapidly increasing incidence of arteriosclerotic and senile illnesses, fresh interest has been aroused relative to the mental diseases of old age. Less attention appears to have been given to the mental problems of the middle-aged group.

The designation of definite age limits for the middle-aged group constitutes in itself a controversial issue. Few people are prepared to admit that they have already strayed from the alluring paths of flamboyant youth to the more conservative highway of middle age, and fewer still will agree that they have begun to descend the hazardous pathway to old age. We may disregard the well-known adage, "Life begins at forty," and for purposes of academic discussion accept the age span of forty to sixty as representing the middle-age period.

Somewhere in this age group, the individual reluctantly awakens to the necessity of abandoning the fearless aggressiveness of earlier years, to rest, only too often, lethargically content in a false sense of self-satisfied complacency, or to permit himself to be weighed down by the depressing outlook of progressively declining physical and mental capacities.

Yet it is in this period that life places on both men and women its greatest responsibilities: maintaining the home, educating the children, meeting social obligations, ensuring economic independence and retaining physical and mental fitness, without which the fulfillment of all these responsibilities inherent to mid-life becomes exceedingly difficult. Persons belonging to this group, according to Kahn and Simmons,¹ "are taken for granted, and apparently they are not supposed to have problems." They add, "In fact they are the people who set out to solve the problems of youth and old age." As they aptly point out, settling other people's difficulties may prove a problem in itself, and may suggest a beam in one's own eye.

Just how complex and overwhelming are the problems of middle age? What are the common pitfalls of this period? These are some of the questions which we shall attempt to answer.

Consider first the responsibilities of the home: food, shelter, clothing and the maintenance of

*From the Ring Sanatorium and Hospital, Arlington Heights, Massachusetts.

†Medical director, Ring Sanatorium and Hospital.

‡Senior assistant psychiatrist, Ring Sanatorium and Hospital.

health,—the very essentials of existence,—not only for the individual himself, but for the marital partner, the offspring and perhaps other dependent relatives. These responsibilities form a constant source of anxiety and worry for the man or woman who has arrived at mid-life and who is expected to provide for them.

It is at this stage of life that the problem of the education of children reaches its peak. The child has matured into manhood, he has reached the college age. It is at this moment that a place must be found for him in the realm of industrial economy. Hence the necessity, often at the cost of much hardship and deprivation on the part of the parents, of procuring for the child the wherewithal to attain these ends.

If we consider the individual from the standpoint of his social obligations, we find that it is between the ages of forty and sixty that society exerts its most pressing demands. It is no longer sufficient for him simply to participate in the various social activities of the community, he is now expected, by reason of having reached the so-called "age of wisdom," to assume a place of leadership in the social field, not only for the benefit of his own age group, but also for the fostering of the social requirements of youth and old age.

Of still greater importance to the person of middle age is the responsibility of assuring economic security, which forces him to face the increasingly pressing realization that there remains only a limited time for the creation of that financial independence which he has only recently come to recognize as a necessity. This problem naturally fosters anxiety and apprehension, which may tend to be in various stages of repression. Furthermore, while he is struggling to ensure the security of his own financial position, he is often confronted with the necessity of helping others to become economically stable. There are, of course, variations in the seriousness of the situation, just as there is a wide difference in the most suitable age for different occupations. For example, the professional athlete is already on the wane in his late thirties, or even earlier, while at the same period of life the professional man—the doctor, lawyer or teacher—has just begun his career. In either case, problems result, with their major assault on the individual within the arbitrary age limits chosen in the present study.

What of the physical changes, with their mental repercussions, inherent in middle age? Biologically, it is in this group that we find the truly "dangerous age." Woman becomes the unfortun-

nate heir to the climacteric, with its well-recognized physiologic and nervous system maladjustments. She is beset by mild or severe depressions, irritability, fear and the knowledge of "having done those things which she ought not to have done, and of having left undone those things which she ought to have done." Man may or may not be subject to a similar physiologic and nervous upheaval, but certainly we frequently see a clinical syndrome closely simulating the female involutional changes, occurring at the stage of life corresponding to the climacterium.

There appears also, at this stage of life, the need for drastic curtailment of physical activities. Those once indulged in freely and with impunity become no longer permissible. In a vain attempt to disregard these limitations, the man of middle age may overtax himself and bring about a state of nervous exhaustion requiring hospital care. On the other hand, if he recognizes the boundaries placed on his activities by the advancing years, he may unwisely drop all physical recreation to the point of finding himself totally without physical outlet, a situation which is hardly conducive to optimal mental health.

The importance, at this crucial age, of the sex factor in the pathogenesis of mental diseases cannot be overestimated. This is particularly true of the neuroses. Phobias, many of them carried over from childhood and adolescence, others peculiar to this age, frequently result in partial or total mental disability. Hidden feelings of guilt resulting from faulty sexual hygiene, the harmful effects of which are so frequently misunderstood and exaggerated, or following sexual indiscretions in the case of physical incompatibility of the marital partners, tend to disturb profoundly the normal mental equilibrium of the individual. Gradual failure of sexual vigor, impotency and fear of impotency, and religious, social and legal barriers to the sexual outlet, following loss of the marital partner, either through death or separation—any of these problems may be operative as the source of the patient's symptoms. The etiologic importance of sex difficulty is only rarely obvious. More often than not, the underlying causal factor will be found to be masquerading under the cloak of one or more of a multitude of clinical manifestations, such as alcoholism, restlessness, agitation, hysteria, neurasthenia, apathy, depression, perhaps leading to self-destruction, excessive erotism, sexual promiscuity and many others. The semeiologic polymorphism characteristic of the sexual problems of these years precludes any attempt at numerical evaluation in as limited a study as the present one.

We have mentioned only some of the problems of the middle-aged group which, when improperly handled, become precipitating factors in the development of nervous and mental reactions that are frequently severe enough to require hospitalization.

It is a well-known fact that most admissions to public institutions treating mental diseases do not fall within the forty-year to sixty-year age limits. On review of the admissions to the Ring Sanatorium and Hospital during 1937, 1938 and 1939, however, we have been interested to find that of a total of 849 patients, 356 (41.9 per cent) were in this group, even though the ages of those admitted

The same reasoning appears to hold good in the drug and alcoholic group. In a sense, a majority of these persons might well be included among those classed as having mental illness, as neurotic and psychopathic symptoms are in great prominence. We have excluded, however, all cases of drug and alcohol addiction without mental symptoms, in order to make the picture clearer and to keep it within well-defined limits.

Among this group of 100 cases, 72 fell within the so-called "functional group"; that is, they failed to reveal any evidence of organic change in the nervous system associated with mental symptoms (Table 1). Twenty-four of these were classified in

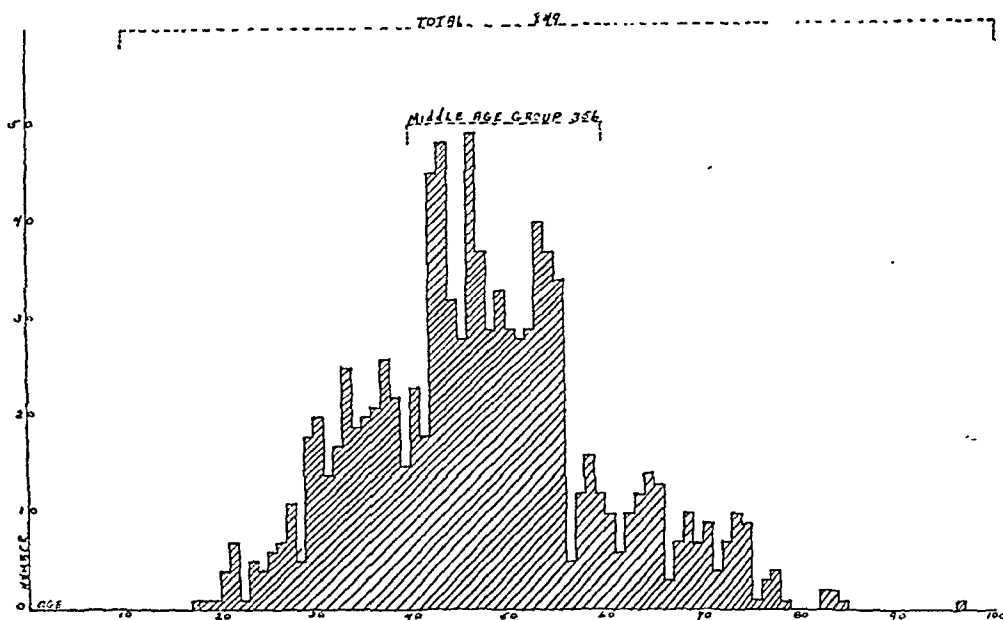


FIGURE 1. Graph Showing the Admissions for 1937, 1938 and 1939 in Relation to Age.

ranged from eighteen to ninety-six. In other words, nearly half the total admissions were in the middle-aged group. However, most of those who came to the sanatorium for the treatment of alcoholism and drug addiction also proved to be within the ages of forty to sixty. These figures, as we have said, include all admissions, but the necessity for fixing some boundaries has caused us to limit the cases to 100 having definite mental symptoms, and occurring in the delineated age group.

What is the reason for the higher admission rate in the middle-aged group, as compared to that reported from public institutions? We offer a two-fold explanation: in view of the unfortunate general attitude toward mental illness, every effort must be directed, at this particular period, toward the protection of the individual from any so-called "stigma"; secondly, it is at this wage-earning period that people are best able to afford this protection.

the manic-depressive group, with 18 in the depressive phase. Involutional melancholia was the accepted diagnosis in 18 of the 72 cases. To the latter classification we have admitted only those patients having symptoms of depression, agitation and self-accusatory ideas customarily associated with the involutional state. We have not included those having a history of previous attack. The psychoneuroses were next in frequency, with a total of 16 cases. Most of these patients had had previous episodes, but the stress of mid-life had again precipitated symptoms requiring institutional care. Schizophrenia was represented by only 6 cases. This is not surprising, since schizophrenia is essentially a disorder of youth. Four cases were labeled psychopathic personality, and 4, paranoid condition.

Among the organic group, 17 cases were represented, the most frequent condition being psychosis

with cerebral arteriosclerosis, which appeared 7 times. General paresis or syphilitic meningo-encephalitis accounted for 4 cases, traumatic psychosis for 2, and Pick's disease, taboparesis, post-encephalitic syndrome, and psychosis with other somatic disease for 1 each.

The remaining 11 cases were divided among the following diagnoses: 2 each of toxic psychosis,

TABLE 1. *Classification of Psychoses.*

DIAGNOSIS	No OF CASES
Functional psychosis	72
Manic depressive psychosis	24
Depressed	18
Manic	6
Involuntional melancholia	18
Psychoneurosis	16
Schizophrenia	6
Psychopathic personality	4
Paranoid condition	4
Organic psychosis	17
Cerebral arteriosclerosis	7
General paresis	4
Trauma	7
Pick's disease	1
Taboparesis	1
Postencephalitis	1
Psychosis with other somatic disease	1
Toxic psychosis	9
Toxic psychosis	2
Drugs	2
Delirium tremens	2
Alcoholic hallucinosis	2
Korsakoff's psychosis	1
Undiagnosed psychosis	2
Total	100

psychosis with drug addiction, delirium tremens, alcoholic hallucinosis and undiagnosed psychosis, and 1 case of Korsakoff's psychosis.

In consideration of the etiologic factors which we have reviewed, we should expect to find depression and its associated phenomena, weeping, self condemnation and somatic complaints, occupying the most prominent place among the symptoms. This proved to be true, with an incidence of 39 cases (Table 2). The next group of symptoms in point of frequency were those in the sphere of agitation, restlessness, irritability and insomnia, which occurred 22 times. Anxiety, worry, apprehension, nervousness and preoccupation also occupied a prominent place, and were given as the initial symptom in 16 cases. Other symptoms were: disturbances of sensorium, such as confusion, failing memory and irrational state, 8 cases; physical symptoms, weakness, headache, parotitis, hemiplegia and tremulousness, 5 cases; obsessions, compulsions and phobias, 5 cases; hallucinations, 2 cases; and exhibitionism, dysphagia and drowsiness, 1 case each. In 7 cases the symptoms were so indefinite that they are of necessity classified in more than one group.

The average hospital residence of the 100 patients was 47 days. A review of their condition on discharge reveals that 13 were regarded as recovered,

54 as greatly improved, and 32 as unimproved; 1 was deceased.

It is interesting to note that suicidal threats were made by 24 patients, and that 6 of these made suicidal attempts, either before or during hospitalization. One successful attempt was made by a patient who had left the hospital without permission. The presence of a history of mental illness in the family antecedents of 20 of these 24 patients, and of a suicidal history in the antecedents of 5, reveals an important hereditary influence.

One cannot stress too much the importance of removing the patient to the friendly atmosphere of a hospital, where close nursing and medical supervision are available at all times. We have shown the preponderance of the depressive states during the mid-life period. Proper supervision of a suicidal patient can best be secured in a hospital where specially trained nurses know the value of constant vigilance.

In the way of therapy, the accepted methods were employed. Special care was given to the

TABLE 2. *Initial Presenting Symptoms.*

SYMPTOMS	No OF CASES
Depression	39
Weeping depression	
Self condemnation	
Somatic complaints	
Hypostactivity	
Blue spells	
Agitation	22
Restlessness	
Agitation	
Irritability	
Insomnia	
Anxiety	16
Worry	
Preoccupation	
Apprehension	
Nervousness	
Confusion	8
Failing memory	
Confusion	
Irrationalism	
Personality change	7
Mood swings	
Paranoid ideas	
Grandiose ideas	
Obsessions	5
Phobias	
Compulsions	
Physical symptoms	
Weakness	
Headache	
Hemiplegia	
Tremulousness	
Parotitis	
Hallucinations	2
Exhibitionism	1
Dysphagia	1
Drowsiness	1
Total	107

physical condition of the patient, and every effort was made to treat and correct any organic disease. Hydrotherapy was used in those cases in which the patient was disturbed, tense, anxious, depressed or excited. We have used the neutral tub bath,

the continuous-flow bath, the cold and neutral wet-sheet pack and the various sprays and douches. The psychotherapy employed was of the suggestive and re-educational types. Occupational therapy, both formal and in the patients' rooms, and outdoor exercise formed important features of the daily schedule. Electrotherapy appeared to be of value, particularly in certain organic conditions, and in some of the psychoneuroses. Special therapy was resorted to for the organic manifestations of general paresis and for the treatment of menopausal symptoms. In general paresis, malarial and artificial fever therapies were used, in conjunction with chemotherapy; while in the menopausal deficiencies, replacement hormonal therapy gave good results. Shock therapy (Metrazol and insulin) was not used in any of the cases of schizophrenia represented in this group, since none were suitable for such treatment.

We present in brief form the essential features of 3 cases regarded as typical of the predominant group: 1 of psychoneurosis, 1 of involuntional melancholia, and 1 of manic-depressive psychosis (depressed).

CASE REPORTS

CASE 1. M.I.M. (No. 4771), a 44-year-old, married woman, was admitted on December 31, 1938, and was discharged on February 18, 1939. There were irritability, loss of strength and many somatic complaints. The family history was negative. The patient's mother died when she was 3½ years of age, and she was brought up by her grandmother. She had had the usual childhood diseases. She had had an appendectomy and a tonsillectomy and adenoidectomy as a child, influenza followed by bilateral lobar pneumonia in 1919 and a right salpingo-oophorectomy in 1937. During adolescence she suffered a fracture of the right arm and of the right second toe. She completed high school and attended a teachers' college for a short period, then studied voice. She was a concert singer in this country and abroad for 15 years. She was married at 28. At first her married life was happy; she then found that her husband was unfaithful and that he was an alcoholic addict. There had been no pregnancies. The patient was described as high-strung, very sensitive and introspective. Her habits were good, except for the use of barbiturates for a number of years.

In 1929, during the financial depression, she became worried, unhappy and run down. She had periods of fainting, then alternating periods of feeling well and feeling ill. Since that time, on three occasions, she had spent periods of 2 to 5 weeks in hospitals. In the 3 years before her admission, her husband had been very neglectful and frequently humiliated her. She described strong feelings of insecurity and shame, and a tendency to shun other people and feel sorry for herself, and stated that she had had friction with her husband's relatives. She felt weak, exhausted and irritable, and complained of pain in various parts of her body.

At physical examination the patient was undernourished. There was definite tenderness over both antrums. The pupils were unequal, the right being greater than the left. The upper jaw was edentulous, and there were several

teeth missing from the lower jaw. There was a pleural friction rub over the right chest. The blood pressure was 164/100, dropping to 144/90. There were old healed operative scars on the abdomen, and there was a slight scoliosis to the right. A blood Wassermann test, x-ray examination of the chest, an agglutination test for undulant fever and a urinalysis were negative. There was a mild secondary anemia.

Mentally the patient was, for the most part, pleasant, but at times she was unstable. There were many hypochondriacal complaints, such as dyspnea, anxiety and a sensation of tightness in the back of the neck. On one occasion she slumped to the floor, following which there were no abnormal findings.

The patient discussed her family problems freely. She expressed feelings of insecurity and a desire to do something for herself, yet she could not decide to extricate herself from the home situation. During the first part of her residence she ran a low-grade fever, which cleared later. She was treated by psychotherapy, sedation, hydrotherapy and electrotherapy, massage and occupational therapy. She improved slowly during her stay in the hospital, and at the time of discharge was greatly improved.

CASE 2. G.B. (No. 4869), a 46-year-old housewife, was admitted on October 4, 1939, and discharged on November 10. She was readmitted on January 7, 1940, and discharged on February 3. The family history was essentially negative. The patient's infancy and childhood were not remarkable. She graduated from high school and attended business college. Immediately following graduation she married a salesman. Her marital life was very happy. There was one daughter about to be married; this the patient resented. The menses had begun at 14, and there had been no abnormality until 1928, at the age of 34, when they became irregular and scanty. Three years later she developed menorrhagia (10 days to 2 weeks). She had continued to be troubled with menstrual dysfunction until the present time. Her last period prior to the first admission continued for 17 days. She was described as cheerful, friendly, sociable and a good mixer. She was interested in sports, her home and social activities.

The present illness began on October 13, 1938. While shopping the patient suddenly responded to an impulse to walk away with a small article from the counter, in the act of which she was discovered. Although she was fully cleared following investigation, she continued to worry and to be self-critical, and said that she was powerless to overcome the shame that she had brought on herself and her family. She gradually became more depressed, restless and agitated, and hospital care was advised. In March, 1939, she was sent to a state hospital, where she remained for 2½ months. There she was depressed and irritable, was considered suicidal and expressed self-accusatory ideas. The sensorium was clear. The patient responded well to injections of follicular hormone; at the time of discharge she was considered much improved. A diagnosis of involuntional psychosis was made. On returning home she continued the use of the hormone for but a short time. Toward the latter part of the summer of 1939 all her mental symptoms returned and she was admitted to the sanatorium in October.

Physical examination was essentially negative, as were laboratory studies, including a blood Hinton test. Mentally the patient was depressed, retarded, self-accusatory and at times agitated. She talked a great deal of the shame she had brought on the family through the shopping incident. She was again given large doses of follicular hormone, and rapidly improved. Her husband

insisted on premature removal on November 10. She was readmitted in January, 1940, for further treatment. During this residence she continued to be depressed, was irritable and did not respond as before to hormone therapy. She was finally discharged in February against advice, still depressed and self-accusatory. This case is quite typical, and shows the type of severe reaction seen in women at the climacterium.

CASE 3 J H B (No 4805), a 43 year old married man, was admitted on April 20, 1939 and discharged on May 9, 1939. The family history was essentially negative. The patient's infancy and childhood were not remarkable. After graduation from high school he went to war, and on returning went into the leather business which his father had established. During the 2 years previous to admission he had recognized signs of insecurity in his position, which he had tried to overcome by attending law school at night. In December, 1938, the firm went bankrupt and he was thrown out of work. He tried various occupations, but was never able to get permanently placed. For 2 months he seemed able to adjust himself fairly well to the situation, but then became increasingly depressed. His first complaint was insomnia, then shaking spells, and finally he became very tense and anxious. He felt guilty because he had accepted help from his father, and became self-critical, agitated, more depressed and retarded. Three weeks before admission he developed a fear that he had syphilis, then feared that his family had it, and finally was sure that everyone in town was infected with it. He was sure that his face was changing, and he would look at himself in the mirror for long periods. Hospital care was advised.

Physical examination revealed a depressed and agitated man, with a blood pressure of 200/130. There was no evident peripheral arteriosclerosis. Blood Hinton and spinal fluid Wassermann tests and urinalyses were nega-

tive. Mentally the patient was agitated and depressed, was self-accusatory and expressed ideas of unworthiness. He retained his obsessions regarding syphilis, and was retarded in speech and thought. Three days after admission he made a suicidal attempt by diving against a radiator. He responded well to hydrotherapy, and gradually by the severity of his symptoms lessened. By May 22, about a month after admission, he expressed serious doubts as to the validity of his obsessions, seemed more cheerful, was more spontaneous and admitted freely that he had made the suicidal attempt. He continued to improve, and on May 29 was discharged with a diagnosis of manic-depressive psychosis (depressed), condition improved. This picture is very similar to that seen in women in the climacteric period, and is quite typical of those symptoms in men in mid life who have undergone serious threats to their security.

These cases are presented as typical of the more severe reactions in mid life. Many of these are comparatively mild, but they have the potentialities of becoming acute.

SUMMARY

The mental problems of the middle aged group are reviewed.

A brief study is presented of 100 such patients between the ages of forty and sixty.

Three case abstracts representing the severe reactions that may be manifested in response to problems in this age period are given.

REFERENCE

- 1 Kahn, E. and Simmons, L. W. Problems of middle age. *Yale Rev* 29: 349-373, 1940.

REPORT ON MEDICAL PROGRESS

THORACIC SURGERY

EDWARD D CHURCHILL, MD*

BOSTON

PULMONARY TUBERCULOSIS

A CONCISE and useful treatise on pulmonary tuberculosis has been published by the Oxford University Press¹ under the joint authorship of an internist, a pathologist and a surgeon. In reviewing this book for the *American Review of Tuberculosis*, Max Pinner² refers to it as "the most usable book on this subject in the English language," and remarks that "the practitioner wishing to find up to date information will find it here in concise and digestible form." As Pinner is not given to the use of superlatives without due cause, his favorable criticism may be taken at its face value. The chapters on the pathology of tuber-

culosis by Pagel are particularly well done and provide an essential background for the clinical management of the disease. This aspect of tuberculosis has on the whole received scant attention in America, mainly owing to the fact that large public institutions housing tuberculous patients have in the past been poorly equipped with personnel and facilities for postmortem studies.

The chapters on the application of surgical measures to pulmonary tuberculosis are highly colored with the dictums of the Sauerbruch school, and many details are at variance with the practice of American surgeons. The recent edition of Alexander's *The Collapse Therapy of Pulmonary Tuberculosis*³ is the authoritative treatise on this phase of treatment. A new volume, *Artificial*

*Felix H. Mans, professor of surgery, Harvard Medical School, Chief of the West Surgical Service, Massachusetts General Hospital.

Pneumothorax,⁴ has recently been issued by the Saranac Lake group, and promises to be a useful and practical reference for physicians interested in this subject.

Collapse therapy is fortunately no longer on trial, but public institutions are from time to time obliged to show justification for the additional expense necessary to maintain an adequate surgical program. A report from the Municipal Tuberculosis Sanitarium of the City of Chicago⁵ records an experience with 7341 patients observed over a six-and-a-half-year period. Three thousand and ninety patients were subjected to collapse for more than three months and 337 for less than three months. In 330 cases artificial pneumothorax was attempted; 3584 patients served as controls. Broadly speaking, the results were twice as good with the treated patients as with the controls, and better still as against the life expectancy of patients with open tuberculosis as revealed in the literature. Collapse is viewed as a treatment sequence, with an ideal indication and an optimum moment for each operation.

This conception of collapse therapy as a treatment sequence is of course extremely significant. It has been expressed by metaphor as a game of chess in which a series of moves is carried out, all directed toward the same purpose. At the present time the move that is most frequently delayed is the shift from a partially successful artificial pneumothorax to a more effective collapse measure. The dangers of continuing an incomplete pneumothorax that has not converted the patient's sputum from positive to negative have been stressed for years, but the surgeon still receives a steady flow of cases of tuberculous empyema that result from such injudicious tactics.

An understanding of the pathology of the disease will also inform the operator regarding the hazards of artificial pneumothorax when it is induced early in the course of a pneumonic type of lesion or in the initial phase of benign hematogenous spread. Tubercles directly beneath the visceral pleura lead to pleural extension and the grave complication of a tuberculous empyema. The patient then becomes the victim of the treatment of the disease rather than of the disease itself.

After an initial experimental phase, the procedure of extrapleural pneumothorax is finding a limited place in the armamentarium of the thoracic therapist. It is a valuable method of treatment, as is intrapleural pneumothorax, and no doubt will be on record where the procedure of lung has taken the place of the quiescent. Many cases have been treated with oil and

nitely. Under these circumstances thoracoplasty must be considered preferable as a primary procedure. Extrapleural pneumothorax is finding its place as a palliative measure or as preliminary to thoracoplasty. With adequate medical therapy it will rarely be needed in the latter capacity. Many reports⁶⁻¹³ on the procedure have appeared in the recent literature.

The goal in the therapy of pulmonary tuberculosis is the conversion of a positive sputum to one that is free of the tubercle bacillus. This requires the obliteration of cavities; and collapse therapy, either with artificial pneumothorax or by surgical measures, is largely concerned with the closure of cavities. As the cavity has become a center of interest in the treatment of the disease, it is not surprising to find that knowledge concerning it has increased and certain new concepts have been developed. In fact, the new science of "speleology" (from the Greek *σπηλαιον*, meaning "cave" or "cavern") has emerged.

The natural healing processes that from time to time bring about the spontaneous obliteration and healing of tuberculous cavities have been described at length by pathologists. Spontaneous healing is, however, such a rare occurrence that, given a demonstrable excavation, no time is lost in applying the active measures of collapse therapy if other indications permit.

It was formerly thought that the spherical shape of a cavity in the lung was a resultant of forces inherent in the elastic tissue of lung substance. It was known that cavities might be larger than the original liquefied caseous areas, and the mechanism involved was pictured by placing a sheet of rubber under tension and piercing it with a pin. The size of the resulting hole depended on the degree of tension to which the rubber was subjected. In certain texts a cavity in the lung was shown in the form of a diagram in which the circular defect was surrounded by small spiral springs arranged radially about the circumference.

In 1930 Pearson¹⁴ demonstrated a high positive pressure within air-containing cavities, an observation that has led to quite a different concept of the mechanical forces involved, and has suggested certain new therapeutic procedures.

Coryllos¹⁵ extended observations on the pressures within air-containing cavities and also inspected their interiors with a small thoracoscope. He attributed the positive pressure to partial bronchial occlusion that acted as a one-way valve. Air under tension entered the cavity in the act of coughing and was trapped so that it could not escape. If the bronchial occlusion became complete, the first manifestation was the appearance of a fluid

level; then, as the air was absorbed by the blood stream, the cavity became smaller, even to complete disappearance. These observations furnished a reasonable explanation for certain puzzling phenomena that had been observed from time to time by many clinicians. Large cavities with thin walls had been observed to appear within a short space of time and to vanish completely in the same abrupt and unexplainable manner. In other cases cavities remained unaltered in size by a complete artificial pneumothorax. Eloesser¹⁶ presented a detailed description of the behavior of "blocked" or ballooned cavities in his presidential address before the American Association for Thoracic Surgery.

It was suggested^{17, 18} that all would be well if a bronchus could be permanently occluded by artificial measures, and experiments with animals were initiated to find a method that could be applied clinically. About this time, however, both internists and surgeons dealing with pulmonary disease developed a wholesome respect for the effects of bronchial occlusion as a spontaneous manifestation of disease processes.^{19, 20} At the present time it is doubtful that anyone would have the temerity deliberately to produce bronchial occlusion in a patient.

A bold and ingenious step has been proposed by Monaldi²¹ for dealing with this type of tuberculous cavitation through a peripheral approach. A catheter is inserted by means of a trocar directly through the chest wall into the lumen of the cavity. Low-pressure suction is applied intermittently. It is reported that cavities so treated immediately decreased in size and became obliterated within four months. Information regarding the Monaldi procedure is based almost entirely on word-of-mouth transmission at the present writing, as well-documented case reports have not yet appeared in the literature. It is, however, a logical outgrowth of changing conceptions regarding the physiopathology of cavitation.

Surgeons are beginning to consider actual extirpation of the lung in selected cases of pulmonary tuberculosis. Of course some of the earliest attempts at lung resection for tuberculosis were carried out between the years 1881 and 1895. These are recounted in treatises by Ruggi²² and by Tuffier.²³ The subject was then dropped, and the highly successful development of collapse therapy removed the stimulus to revive what was obviously a hazardous and difficult undertaking. Two things have now happened: first, resection of the lung for other diseases has brought technical improvement and familiarity with the operation; secondly, the

failure of collapse therapy in certain phases of pulmonary tuberculosis can be predicated.

In 1934, Freedlander²⁴ reopened the question in an address to the American Association for Thoracic Surgery, and several discussers added cases from their own experience. These cases as a rule were ones in which resection was undertaken for what was supposed to be bronchiectasis but what subsequent microscopy identified as tuberculosis. It soon became apparent that the patients did not die of generalized tuberculosis, nor did their incisions fail to heal or bronchial fistulas persist. At the present time, therefore, pulmonary resection is seriously considered and not infrequently undertaken in known tuberculous pulmonary infection when there is a serious degree of bronchial stenosis that precludes success with collapse therapy. It has also been performed for large areas of caseation and liquefaction that have not found a bronchial outlet, and is proposed for cavities so situated that the likelihood of being able to collapse them by chest-wall surgery is slight. The latter indication may well be a pitfall for the enthusiast, and should be entertained only by a surgeon thoroughly familiar with modern methods of collapse therapy.

PRIMARY CARCINOMA OF THE LUNG

Reasons for the recent increase in the incidence of bronchial carcinoma were discussed by Boyd²⁵ in the 1938 Mütter Lecture of the College of Physicians of Philadelphia. During the ten-year period ending in 1936, at the Department of Pathology of the University of Toronto, the third most frequent site of primary cancer was the lung. It was exceeded in frequency only by the stomach and large bowel. The actual incidence was 1.2 per cent in 4500 autopsies. In Winnipeg the incidence was 2.6 per cent in 2408 autopsies.

The increased incidence of primary carcinoma of the lung has been a world-wide phenomenon. Explanations have been sought on the supposition of the inhalation of a carcinogenic agent. The tarring of roads and the dissemination of automobile exhaust gases are commonly cited. Boyd points out that in Winnipeg tarred roads are remarkable for their absence and that in Russia there are practically no tarred roads and few automobiles; also that in Beirut, Syria, carcinoma of the lung is as common as it is in Philadelphia, yet the patients live as did their forefathers in the days of the Pharaohs. He defends the thesis that knowledge of the disease has spread over the world and is the most important element in the apparent increased incidence, and quotes MacCallum as follows regarding syphilitic aortitis: "Since

then everyone has recognized it at a glance. It seems to be one of those simple triumphs of observation that makes one ashamed of being so blind."

According to Boyd, there is no form of tumor more easily overlooked, especially if the case does not come to autopsy. The clinical diagnosis is difficult because the disease may be so long latent or occult, and because metastases frequently dominate the picture. The radiologist has learned to observe not the tumor itself but its effects in the thorax. It is more difficult to explain the fact that the leading pathologists of the nineteenth century failed to recognize it, if it really was common in those days.

The failure of pathologists to recognize primary cancer of the lung Boyd attributes to ignorance of the nature of the gross lesion, of the microscopic picture and the natural history of the disease, that is, the methods of spread and the sites of metastases. Numerous mistakes of his own department are cited. He concludes, "What we know, we see." This has been true of coronary thrombosis and is true of bronchial carcinoma. It is true for the clinician, the bronchoscopist, the radiologist and the pathologist.

Boyd's analysis is comforting to those of us who drive automobiles over tarred roads and light cigarettes at the traffic lights, because experiments with mice show that the exposure to carcinogenic agents does produce an increased incidence of pulmonary tumors. According to Campbell,²⁶ inhalation experiments prove that cigarette smoke gives a high incidence of lung tumors in mice as compared with controls. Soot from automobile exhausts suspended in the atmosphere gives a slight increase in the incidence, and dust from tarred roads appears to be a significant and dangerous source of carcinogenic agents.

Elaborate consideration of the statistical evidence purporting to show an actual increase in the incidence of primary pulmonary cancer may be found in a monograph compiled by Simons.²⁷

A few years ago Pancoast²⁸ described a symptom complex produced by a malignant tumor invading the extreme apex of the thoracic cavity, or, as he called it, the superior pulmonary sulcus. A tumor in this region, he said, produces pain referred to the shoulder, arm and hand, associated with partial paralysis due to invasion of the lower cords of the brachial plexus; paralysis of the cervical sympathetic nerves, manifested by Horner's syndrome²; and evidence by x-ray of destruction of the upper ribs or vertebrae. Pancoast postulated a specific tumor arising from an epithelial (branchial)

²Priority rights regarding this eponym are under discussion at present. It has been suggested that the term "Hare's syndrome" should be substituted (Fulton²¹ and Morris and Harken²⁹).

rest as the cause of the syndrome. It is now apparent that the symptom complex described by him is not a specific one, as it may be produced by a variety of tumors of different origins. The symptom complex is not an uncommon manifestation of primary carcinoma of the lung, and most of the cases encountered clinically are of this nature.

A matter of definition in regard to terminology is raised by Morris and Harken.³⁰ It is pointed out that Pancoast postulated a "lack of origin from lung, pleura, ribs or mediastinum." A Pancoast tumor is therefore not to be confused with the superior-pulmonary-sulcus syndrome that it produces and that is admittedly nonspecific. If it can be definitely established that a squamous-cell epithelioma arises from a cell rest in this region and produces the symptom complex described, the Pancoast eponym may be perpetuated, but it must be confined to this specific entity. Tumors of pulmonary or other origin should not be termed "Pancoast tumors" even though the superior-pulmonary-sulcus syndrome is produced. Morris and Harken believe that they can identify three true Pancoast tumors among 8 cases of apical cell tumor.

The number of cases of carcinoma of the lung that can be salvaged by surgery remains disappointingly low. Tudor Edwards³¹ reports 172 cases of bronchogenic carcinoma that came under observation in two and a half years. Of these 28 were submitted to thoracotomy as possibly resectable. In 13, dissection pneumonectomy was carried out. Six patients survived after operation from six months to two and a half years. These results very closely approximate the unpublished figures of the Massachusetts General Hospital, are of value in giving a broad view of this disease. Benign bronchial adenoma is still being confused with primary bronchogenic carcinoma particularly in regard to reporting the results of surgical treatment. As I³² have stated elsewhere:

During the ten-year period ending April 1, 1949, clinical diagnosis of primary tumor of the lung made in 380 cases at the Massachusetts General Hospital. It was confirmed by microscopic examination in 172 cases, of which 155 are classified as primary bronchogenic carcinoma, 15 as adenomas or carcinoids, neurofibroma and 1 as hamartoma. The frequency of benign tumors in the entire group is but 4.4 per cent, a relatively insignificant number. The frequency calculated for the group with microscopic confirmation of the diagnosis rises to 10 per cent. If attention is directed to the group in which resection was carried out it is found that benign lesions account for approximately 30 per cent of resectable bronchogenic tumors. Consideration is still further limited to patients surviving resection with apparent arrest of the disease, be-

lesions comprise 64 per cent. These figures are cited to show how important it is for surgeons and pathologists to agree in their definitions before comparing results in the treatment of pulmonary neoplasms.

Improvement in the treatment of carcinoma depends on early diagnosis. Hochberg and Lederer³² have studied the early manifestations of primary carcinoma of the lung. In 21.6 per cent of cases, the first symptoms that brought the patient to the physician did not suggest intrathoracic new growth. In 10 of 18 cases in which the diagnosis was not established until one to six months had elapsed after first medical advice, the correct diagnosis would have been made if the physician had thought of the fact that infradiaphragmatic symptoms may be due to supradiaphragmatic disease, or if in suspicious cases bronchoscopic examination had been suggested.

In the earliest important monograph on primary malignant growths of the lung, published in 1912, Adler³⁴ wrote:

As at the present the conscientious physician examines every chest for possible tuberculosis, so in the future every chest will have to be examined for possible tumor. The writer would go still farther. Where all the means of diagnosis outlined in this little study fail, where there is suspicion of tumor, but no assurance is possible, there should be—it is emphatically here stated—as little hesitation in resorting to an exploratory thoracotomy as there is nowadays in submitting to an exploratory laparotomy.

CYSTS OF THE LUNG

An extensive literature on cystic disease of the lung has accumulated. The terminology is still confused, and a basic difficulty is encountered in differentiating cysts that are true embryologic malformations from those that are the end product of infection. Multiple cysts merge with what may be termed cystic bronchiectasis. Blebs that develop in emphysema may also be confused with other types of cysts.

Sante³⁵ provides an excellent bibliography of the subject, and the following suggestions as to terminology agree in part with his classification.

Congenital cyst a cyst in which there is absolute proof of a congenital origin of the lesion or an unmistakable anomaly of architecture can be demonstrated.

Cyst, a term limited to collections of fluid formed by partial or complete occlusion of secretory glandular structure. Bronchogenic cysts may be intrapulmonary or mediastinal.

Pneumatocele an air-filled cavity. A cyst becomes a pneumatocele with evacuation of its contents.

Bulla: an air-containing bleb arising as a result of emphysema.

Cystic bronchiectasis a borderline entity between multiple-cyst formation and saccular bronchiectasis, combining certain characteristic features of both. Reisner and Tcherkoff³⁶ believe that this is a well defined entity and conjecture a congenital origin. Attention is called to a disproportion between the paucity of subjective symptoms and extensive pulmonary changes. This condition appears similar to the *Waben-lunge* of the German and the "honey-comb" lung described by English pathologists.

Sequestration pneumatocele. Necrotizing infections may leave a large air-filled defect as a legacy. After the infection has burned out, the term "chronic lung abscess" hardly seems applicable. There may be no symptoms, or only an occasional hemoptysis. With the episode of acute infection buried in the childhood history, these may by error be assigned a congenital origin. The original infection is usually a putrid lung abscess or rarely a Friedlander-bacillus pneumonia.

Saccular bronchiectasis. When bronchial stenosis is present the obstructed bronchi may dilate to form large cysts. At times episodes of infection may break down their walls so that intercommunications exist. This condition is usually associated with a very foul sputum due to putrefaction of the retained secretions. If free bronchial drainage becomes re-established the symptoms may be relieved, leading to a classification as cystic bronchiectasis, or the postulation of a congenital origin.

A pneumatocele originating either from a congenital cyst or as the end result of sequestration may contain air under pressure. If it is large, some pneumatoceles occupy the entire hemithorax, — the *sublocative symptoms of a pressure pneumothorax* may be produced. Kaltreider and Fray³⁷ have studied the pathologic physiology of pulmonary cysts and emphysematous bullae.

WOUNDS OF THE LUNG AND PLEURA

It is of timely interest to refer to the subject of chest injuries as one of the most pressing problems of military surgery. Practically nothing can be learned of what is going on in the present European war, except that it may be inferred that the rapidly moving battle fronts have necessitated far-reaching changes in all methods of handling the wounded. In reviewing the experiences of the World War of 1914-1918 basic principles referable to the management of chest wounds are apparent.

In 1918, Lieutenant-Colonel Lincoln Davis and Major Frederick C. Irving were stationed at Limbriaga, Italy, as near neighbors of Ospedaletto 79,

attached to the 11th Corps of the Italian Army during final action on the Piave. Directing this hospital was Major Eugenio Morelli, a pupil of Professor Carlo Forlanini, the originator of artificial-pneumothorax therapy. Morelli had given careful thought to the problems presented by wounds of the chest, and had as a particular contribution proposed the induction of artificial pneumothorax to control hemorrhage from the wounded lung. If hemothorax was present, the blood was aspirated and replaced with air. These propositions, according to Forlanini, had been formulated by Morelli several years before the war, and in fact published in 1910 in a thesis for *Libera Docenza*.³⁸ Davis and Irving³⁹ were so impressed by the methods they observed in actual use by Morelli that they found time to translate his monograph from the Italian. I have had a long acquaintance with this book as it first aroused my interest in thoracic surgery. It is highly recommended to anyone who desires to obtain a more detailed account of the subject.

The immediate mortality in chest wounds from high-explosive missiles is very great. Sauerbruch⁴⁰ examined the dead on the battlefield and found that approximately 33 per cent had succumbed to chest injuries. Duval⁴¹ said that the mortality at dressing stations was very nearly 30 per cent, in ambulances 25 per cent and at army hospitals 15 per cent. Grégoire and Courcoux⁴² gave the mortality as 25 per cent at dressing stations, 20 per cent in ambulances and 2 per cent at hospitals. Duponchel⁴³ reported a 30 per cent mortality at dressing stations and a 34 per cent one in ambulances. Any attempt to reduce the mortality rate of this type of chest wound must therefore be made as near the front line as possible. The matter is made more difficult by the fact that the mortality rate of non-penetrating wounds of the chest wall and penetrating wounds by bullets is low; these should be handled by conservative measures. Accurate appraisal of the situation and prompt treatment of the urgent cases are required just where facilities for careful examination and treatment are most difficult to establish and maintain.

It is impossible to give aid to any appreciable number of wounded dying of massive hemorrhage from injuries to the large vessels. A common cause of death that may be relieved even in a first-aid station, however, is pressure pneumothorax. It is reported that deaths occur from the failure to recognize and relieve promptly the suffocation resulting from this complication of penetrating injuries of the thorax. The treatment is as simple as a tracheotomy: the insertion of a

cannula between the ribs to provide a vent for the accumulating air.

The hazards of chest-wall wounds that penetrate the pleura and produce a "sucking" pneumothorax are well known. These defects must be closed immediately, either with through-and-through sutures or with an occlusive dressing. Arthur T. Cabot is said to have devised the use of a sheet of rubber dam for this type of occlusive dressing.⁴⁴ A more complicated appliance is the inflatable rubber balloon of Morelli.

Injuries that require a formal débridement, with or without the removal of foreign bodies, should be handled as near the front line as facilities for major surgical procedures can be provided. These wounded do not withstand transportation. The dangers of continuing hemorrhage, anoxemia, pressure pneumothorax and pneumonia are immediate and of grave import. A major difficulty lies in the limited number of surgeons trained in the diagnosis and operative technics of endothoracic surgery. An experienced thoracic surgeon can, if circumstances demand it, carry out a débridement of this type without differential pressure anesthesia, as shown by Duval⁴⁵ and by Nissen.⁴⁶ A surgeon unfamiliar with thoracic mechanics is apt to have his own equilibrium disturbed by the terrifying blasts of air that emerge from the chest and the violent motions of the heart and mediastinum, with the result that débridement is inadequate and the stage is set for infection. Differential pressure anesthesia can be administered with a simple apparatus by means of tracheal intubation, and if this could be made available the surgical problems would be immeasurably simplified. It is believed, therefore, that the management of chest wounds may be materially aided by providing trained anesthetists close to the front. This can be done in a much shorter time than it takes to provide an adequate number of surgeons experienced in chest surgery.

ANATOMY OF THE LUNG

The detailed structure of the bronchial tree and the intricate ramifications of the pulmonary blood vessels have become matters of everyday practical importance in the diagnosis and surgical treatment of pulmonary disease. It is impossible to present a résumé of this subject without reference to anatomical sketches and extensive descriptions. For these the reader must consult original sources.⁴⁷⁻⁵¹ As in all other anatomical studies, a first-hand knowledge by actual dissections is required to establish an adequate working basis for precise surgery.

The bronchopulmonary segment, from the stand-

point of roentgen diagnosis and surgical dissection, is the gross unit of lung structure. The limits of these segments are sharply marked on the periphery by injection technics, and their relations to the surface anatomy of the chest wall can be defined within approximate limits. Variations in respiratory excursion, changes in the position of the diaphragm and disease processes in the lung itself all tend to distort the normal topography. A bronchopulmonary segment of the lung is also for all practical purposes a vascular segment, since the number and size of vessels crossing segmental lines in the periphery are relatively insignificant. As the hilar region is approached these anastomosing channels occur with increasing frequency.

At the present time there exists some disparity in the terminology used to designate individual bronchovascular segments and tertiary bronchi. The anatomic pattern itself, however, is far more constant than was formerly believed.

ESOPHAGUS

A complete review of recent advances in the surgery of the esophagus has been compiled by Bird⁵¹ and has been published with an appended bibliography of 677 references. There is no reason to add further comment regarding this important phase of thoracic surgery. It is well to bear in mind the fact that progress is being made in the hitherto discouraging field of carcinoma of the esophagus, and that every clinic which is concerned itself with the surgical treatment of this disease is collecting an impressive series of encouraging results.

REFERENCES

PULMONARY TUBERCULOSIS

- 1 Kayne G O, Pagel W and O'Shaughnessy L. *Pulmonary Tuberculosis Pathology, diagnosis, management and prevention*. 565 pp. New York: Toronto & London: Oxford University Press, 1939.
- 2 Pinner M. abstract *Am Rev Tuberc* 41:128 1940.
- 3 Alexander J. *The Collapse Therapy of Pulmonary Tuberculosis*. "O" pp. Springfield: Charles C. Thomas, 1937.
- 4 Packard E. N., Hayes J. N., and Blanchet S. F. *Artificial Pneumothorax Its practical application in the treatment of pulmonary tuberculosis*. 300 pp. Philadelphia: Lea & Febiger, 1940.
- 5 Rice F. and Hruby A. J. *Collapse therapy in Chicago Municipal Tuberculosis Sanitarium: critical study of eight thousand and eighty-three cases*. *J A M A* 113:101 108 1939.
- 6 Belsey R. *Extrapleural pneumothorax*. *J Thoracic Surg* 7:575 590 1938.
- 7 Overholt R. H. and Tubbs O. S. *Extrapleural pneumothorax in the treatment of pulmonary tuberculosis: preliminary report*. *J Thoracic Surg* 7:591 604 1938.
- 8 Jounides M. and Schlack O. C. *Axillary approach for extrapleural pneumothorax and pneumothorax*. *Am Rev Tuberc* 42:76-81 1940.
- 9 Proctor, O. S. *Four years experience with extrapleural pneumothorax and oleothorax*. *J Thoracic Surg* 9:392 412 1940.
- 10 Paxton J. R., Churchill A. S. and Skillen J. *Extrapleural pneumothorax and oleothorax*. *Am Rev Tuberc* 41:163 176 1940.
- 11 Newton H. P., Dawson F., and Dunphy J. E. *Extrapleural pneumothorax: twenty-one patients treated from November 1937 to March 1938*. *Am Rev Tuberc* 41:319 333 1940.
- 12 Doley F. S., Jones J. C. and Skillen J. *Extrapleural pneumothorax*. *Am Rev Tuberc* 41:403-422 1940.
- 13 Churchill E. D. *Extrapleural pneumothorax*. *Am Rev Tuberc* 41:423 425 1940.

- 14 Pearson S. A. *The pathogenesis of pulmonary cavities*. *Brit M J* 1:330 1930.
- 15 Coryllor E. N. *The importance of atelectasis in pulmonary tuberculosis: its relation to fibrosis and to pathogenesis and healing of tuberculous cavities*. *Am Rev Tuberc* 28:126 1933.
- 16 Eloesser L. *Blocked cavities in pulmonary tuberculosis*. *J Thoracic Surg* 7:122 1937.
- 17 Adams W. E. and Vorwald A. J. *The treatment of pulmonary tuberculosis by bronchial occlusion: experimental study*. *J Thoracic Surg* 3:633 666 1934.
- 18 Custer E. C. and Wood C. B. *Studies on endotracheal occlusion on*. *Surg Gynec & Obst* 59:501 512 1934.
- 19 Lord F. T. *Certain aspects of the diagnosis of bronchostenosis*. *J Thoracic Surg* 1:573 580 1932.
- 20 Eloesser L. *Bronchial stenosis*. *J Thoracic Surg* 1:194 213 1931.
- 21 Doley F. S. *Transpleural aspiration of tuberculous cavities (Monaldi)*. *Am Rev Tuberc* 41:661 663 1940.
- 22 Ruggeri G. *La tecnica della pneumotomia nell'uomo* (8 pp). Bologna: N. Zanichelli, 1885.
- 23 Tuffier *Chirurgie du poulmon en particulier dans les casernes tuber culuses et la gangrene pulmonaire*. 174 pp. Paris: Masson et Cie, 1897.
- 24 Freedlander S. O. *Lobectomy in pulmonary tuberculosis: report of case*. *J Thoracic Surg* 5:132 142 1935.

PRIMARY CARCINOMA OF THE LUNG

- 25 Boyd W. *Some reasons for the recent increase of bronchial carcinoma*. *Col & Sind Coll Physicians Philadelphia* 6:317 328 1939.
- 26 Campbell J. A. *Carcinogenic agents present in the atmosphere and incidence of primary lung tumours in mice*. *Brit J Exper Path* 20:122 132 1939.
- 27 Smoot E. J. *Primary Carcinoma of the Lung*. 263 pp. Chicago: The Year Book Publishers, 1937.
- 28 Pancoast H. K. *Superior pulmonary sulcus tumor: tumor characterized by pain, Horner's syndrome, destruction of bone and atrophy of hand muscle*. *J A M A* 99:1391 1396 1932.
- 29 Fulton J. F. *Horner and the syndrome of paralysis of the cervical sympathetic*. *Arch Surg* 18:205 209 1929.
- 30 Morris J. H. and Harken D. E. *The superior pulmonary sulcus tumor of Pancoast in relation to Hare's syndrome*. *Ann Surg* 112:121 1940.
- 31 Edwards T. *Carcinoma of the bronchus*. *Proceedings of the Eleventh Congress of the International Surgical Society*. Vol 2. Bruxelles: Medical et Scientifique Societe, 1939. Pp. 529 534.
- 32 Churchill E. D. *Resection of the lung*. *Surgery* (in press).
- 33 Hochberg L. A. and Lederer M. *Early manifestations of primary carcinoma of the lung*. *Arch Int Med* 63:80-99 1939.
- 34 Adler I. *Primary Malignant Growths of the Lungs and Bronchi*. 325 pp. New York and London: Longmans, Green & Co., 1912. P. 108.

CYSTS OF THE LUNG

- 35 Sante L. R. *Cystic disease of the lung*. *Radiology* 33:152 165 1939.
- 36 Reisser, D. and Thierhoff I. G. *Cystic bronchiectasis: a clinical and roentgenologic study*. *Am J Roentgenol* 43:327 345 1940.
- 37 Kaltreider N. L. and Fray W. M. *Pathological physiology of pulmonary cysts and emphysematous bullae*. *Am J M Sc* 197:62 77 1939.

WOUNDS OF THE LUNG AND PLEURA

- 38 Cited in *Introduction to Morrell*.³⁹
- 39 Morrell E. *The Treatment of Wounds of Lung and Pleura Based on a Study of the Mechanics and Physiology of the Thorax*. *Artificial pneumothorax—thoracostomy—treatment of emphysema*. Translated by Lincoln Davis and Frederick C. Irving. 214 pp. Boston: W. M. Leonard, 1920.
- 40 Sauerbruch F. *Die Chirurgie der Brustorgane*. Vol 1. 931 pp. Berlin: Julius Springer, 1920. P. 459.
- 41 Duval P. cited by Morrell.³⁹
- 42 Gregoire and Courcoux cited by Morrell.³⁹
- 43 Dupouchel cited by Morrell.³⁹
- 44 Fernald F. C. *Pneumotomy for emphysema recovery*. *J A M A* 7:619 622 1886.
- 45 Duval P. *Les plaies de guerre du poulmon: notes sur leur traitement chirurgical dans la zone des armees*. 139 pp. Paris: Masson et Cie, 1917.
- 46 Nissen R. personal communication.

ANATOMY OF THE LUNG

- 47 Nelson H. P. *Postural drainage of the lungs*. *Brit M J* 2:251 255 1934.
- 48 Neil J. H., Gilmour W., and Wynne F. J. *The broncho-pulmonary segments: radiological, pathological and bronchoscopic considerations with special reference to the subapical broncho-pulmonary segment*. *M J Australia* 2:165 172 1937.
- 49 Neil J. H., Gilmour W., Wynne F. J., Main W., and Ja. *elough W. A. The anatomy of the bronchial tree and its clinical application*. *Australian & New Zealand J Surg* 8:118 131 1938.
- 50 Churchill F. D. and Belsey R. *Segmental pneumonectomy in bronchiectasis: the lingula segment of the left upper lobe*. *Ann Surg* 109:481 499 1939.

ESOPHAGUS

- 51 Bird C. E. *Recent advances in surgery of the esophagus*. *Surgery* 6:11* 637, 7:2 801 949 975 1939.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 26411

PRESENTATION OF CASE

First Admission. A sixty-four-year-old white widow entered the hospital complaining of weakness, apathy and loss of weight.

The patient had been vigorous and healthy until four years prior to admission, when she began to suffer from exhaustion. She had swollen "glands" in the neck with a high temperature. After two months in bed and rest in the country she improved somewhat. She entered an outside hospital for study and was treated for hypothyroidism, requiring 12 gr. of thyroid daily at first, later 2 gr. She was operated on for tuberculous lymph nodes in the neck. One year before admission she had another lymph node of the neck removed. Six months later she entered a Boston hospital where a complete study was essentially negative. Insulin therapy to help her put on weight was immediately followed by rather severe reactions. Soon after this, she complained of shortness of breath, exhaustion and stiffness in the back of the neck. There was a loss of weight of 16 pounds during the last year. She had no appetite and complained of a burning sensation in the right upper quadrant. Her daughter stated that she had no interest in anything, and that she would sit for long periods of time hardly talking or moving. She did not sleep well. She had had the menopause at the age of forty-eight. The diet was very meager in every respect. The past history revealed that she had had "peritonitis" thirty years before admission. One brother died at forty-five of "a neglected cold."

Physical examination by her physician about five months before entry showed a poorly developed and markedly undernourished apathetic woman. There was a yellowish color to the skin. Examination of the head was negative. The thyroid gland was normal to palpation. The chest was normal except for diminished expansion on the right. The systolic blood pressure was 80; the diastolic could not be read. The breasts were normal. Abdominal examination was negative. There was no edema, but the left leg appeared to be larger than the right. The knee jerks were active, but the right appeared to be somewhat more active than the left.

The urine was negative except for an occasional hyaline cast. The blood showed red-cell counts ranging from 4,500,000 to 5,500,000, and a white-cell count of 9800 with 51 per cent polymorphonuclears, 39 per cent lymphocytes, 6 per cent mononuclears and 1 per cent eosinophils. The total base in the blood was 146.5 milliequiv. per liter, and the sodium 137.8 milliequiv. The serum protein was 5.7 gm. per 100 cc.

Her physician prescribed a full diet, graded exercise, and three 15-gr. capsules of sodium chloride with each meal. She improved for a while and gained a slight amount of weight, and the blood pressure rose to 117 systolic, 85 diastolic. When she began to follow her regime less strictly, her condition became less satisfactory. She was then sent to a nursing home, where thyroid, yeast, salt and amphetamine were given. She showed marked improvement, but after a few weeks, she again began to fail.

Physical examination on entry showed an undernourished woman weighing 90 pounds. Examination of the head and chest was negative. The blood pressure was 100 systolic, 80 diastolic. The abdomen was normal.

The temperature was 98.6°F., the pulse 60, and the respirations 20.

Examination of the urine showed a specific gravity of 1.010, a trace of albumin, and no sugar, acetone or bile; there were 25 white cells per high-power field, with frequent small clumps. A urine culture showed staphylococci and a few colon bacilli. There was no follicle-stimulating hormone (prolan A) in the urine. The blood showed a red-cell count of 4,250,000 with 80 per cent hemoglobin, and a white-cell count of 9800 with 56 per cent polymorphonuclears, 25 per cent small lymphocytes, 17 per cent mononuclears, 1 per cent eosinophils, 1 per cent basophils; the smear was normal. The fasting blood sugar was 84 mg. per 100 cc. The basal metabolic rate was -17 per cent. A stool examination was negative for fat.

X-ray films of the skull showed that the bones of the vault were rather heavy and dense. There was some increase in vascular markings on both sides, but there was no evidence of increased intracranial pressure. The sella turcica was normal in size and shape. The pineal gland was calcified and in the normal position. There was no definite evidence of intracranial disease. Plain films of the abdomen were negative.

Pituitary injections and thyroid, salt and vitamin therapy were given. She was discharged on the seventh hospital day.

Final Admission (one week later). Following discharge the patient had run a steady downhill course. Physical examination was essentially un-

changed except for more marked weakness and emaciation. The temperature was 102.5°F, the pulse 65, and the respirations 20. The urine showed a large trace of albumin and innumerable white cells. The blood showed a red cell count of 4,000,000 with 70 per cent hemoglobin, and a white cell count of 12,300. Terminally she went into coma. The blood pressure dropped to 75 systolic, 0 diastolic. The temperature rapidly rose to 106°F., and she died on the third hospital day.

DIFFERENTIAL DIAGNOSIS

DR ALFRED O. LUDWIG: This is the story of a sixty-four-year-old woman who was apparently suffering from some disease that caused her progressively to lose strength and weight, and also to become apathetic and somewhat depressed. The first thing of interest is the history of swollen lymph nodes in the neck. I do not know whether they were proved to be due to tuberculosis, but one would be led to think so. One is told that she was operated on for tuberculous glands of the neck, although we do not know whether it was a postoperative or preoperative diagnosis. At the same time it was thought that she had thyroid deficiency because of the low metabolic rate, and possibly because of other signs. She then had recurrent attacks of difficulty with the lymph nodes in the neck and had to be operated on again.

Another interesting point is that the administration of insulin was immediately followed by a rather severe reaction. That could take place in a number of different conditions. Such insulin reactions occur in patients who are emaciated and have lost weight from any cause, but particularly in those who have deficiency of the anterior lobe of the pituitary gland, or of the adrenal cortex.

The symptoms of shortness of breath on exertion, stiffness in back of the neck, and loss of weight do not help much in classifying the disease from which the patient was suffering. There is no evidence that she had tuberculosis elsewhere except in the neck. There is nothing here to tell us what was the nature of the peritonitis thirty years before. We do not know what happened to her brother; the "neglected cold" may have been pulmonary tuberculosis, but we have no way of knowing that.

Physical examination five months before she came into the hospital showed only loss of weight and a diminished expansion on the right side of the chest. These symptoms may mean old pulmonary tuberculosis with some fibrosis on the affected side. The left leg appeared to be larger than the right. I do not know what this means. The left leg may have appeared to be larger than

the right because of atrophy of the muscles on the latter side; possibly there was a thrombophlebitis on the former side to account for the slight increase in size. I am inclined to discount the information about the knee jerks being more active on the right side than on the left, because we have no evidence of the presence of any other abnormal reflexes on the right side which might lead us to suspect a neurologic disturbance.

There was no significant anemia at this time. The smear and white cells appeared to be within normal limits. Apparently a diagnosis of adrenal insufficiency was suspected because determinations of total base and sodium were carried out. All these levels are a little low, but still within normal limits. The low serum protein might be accounted for on the basis that the patient had been on insufficient intake of protein. Treatment was prescribed with a diagnosis of adrenal insufficiency in mind, and the patient was given sodium chloride. We have no information as to whether she was given adrenocortical extract, but she did seem to improve somewhat, with a slight gain in weight and an increase in blood pressure. This improvement did not last very long, however. The patient continued to lose weight, and the blood pressure again fell.

On the next admission evidence of urinary infection appeared. The most important statement I have so far noticed is that there was no follicle-stimulating hormone in the urine. In women past the menopause there is an increase in this hormone in the urine which persists throughout life. I should say that this was an extremely important finding which in this case might point, and I think does point, to a disturbance of the anterior lobe of the pituitary gland. On this admission the patient showed a slight anemia which was normochromic in type, as confirmed by the normal smear. The white cell counts were within normal limits. She had a low blood sugar level and a low basal metabolic rate at that time. Apparently there was no pancreatic hyposecretion, at least insofar as fat metabolism was concerned, as shown by the absence of free fat in the stool. I wonder if we might see the x-ray films at this time.

DR RICHARD SCHATZKI: The roentgenograms of the skull are not here. The only ones we have are two flat films of the abdomen, which show no unusual mass. There are two areas of calcification on the left side. One could conceivably be in the adrenal gland, but with the other present at the same time I doubt if either is in the gland. They are possibly in the spleen or lower portion of the lung behind the diaphragm. Otherwise there is nothing that would interest you; just changes due to age.

DR. LUDWIG: What about the condition of the bone? Is there any evidence of decalcification?

DR. SCHATZKI: How old was the patient?

DR. LUDWIG: Sixty-four.

DR. SCHATZKI: There is evidence of sclerosis and of degenerative changes of the lumbar spine, but if I had to judge the age of the patient by looking at the bones I believe I could come out quite accurately.

DR. LUDWIG: There is no evidence of decalcification?

DR. SCHATZKI: Not an unusual amount.

DR. LUDWIG: It sounds as though the patient always had this type of skull. I interpret the final episode as being caused by progressive urinary infection with increase in temperature and finally coma and death. The main problem narrows itself down to the cause of this woman's loss of weight and general emaciation, low blood pressure, low metabolic rate, low blood-sugar level and abnormal sensitivity to insulin. Almost all these findings occur in the presence of adrenal insufficiency, but I should think that if she had adrenal insufficiency for this length of time, this woman would probably have had pigmentation of the skin and mucous membranes which, so far as we know, was not present. All the other findings would be perfectly consistent with adrenal insufficiency. I do not know about the absence of prolan A in the urine, but I do not believe this occurs in adrenal insufficiency. On the other hand, an insufficiency of the secretion of the anterior lobe of the pituitary gland could also cause all these phenomena, because this gland contains a very large number of hormones—I think there are about ten now. One is prolan A; another, thyrotropic hormone, the absence of which might be responsible for the lowering of the metabolic rate; another, an adrenotropic hormone, the absence of which might be responsible for some of the symptoms referable to insufficiency of the adrenal gland; and another, a parathyrotropic hormone, in the absence of which there might be some changes in the bone. Loss of secretion of the anterior lobe might well be responsible for all the disturbances in this case. In addition, increased sensitivity to insulin is well known in cases of pituitary insufficiency, particularly in Simmonds's disease. The cases that Simmonds¹ described usually occur in women shortly after the puerperium, and were due to embolism or thrombosis of the nutrient artery of the pituitary gland, with secondary atrophy of the gland. So far as we know this woman certainly had no active thrombophlebitis in the course of her illness. On the other hand she did have tuberculous lymph nodes

in the neck with secondary infection and terminal urinary infection, but I do not think that these played a part in any changes that might have taken place in the pituitary gland.

I believe that the patient did have an insufficiency of the anterior lobe of the pituitary gland, probably secondary to atrophy, the cause of which I do not know. Whether it was due to tuberculosis or to vascular changes with disturbances of circulation and nutrition of the gland I have no way of determining. I do not believe that she had Addison's disease.

DR. ROBERT S. PALMER: I saw the patient during the last year of her life and made tentative diagnoses of involutional melancholia and adrenal insufficiency. She had progressive loss of weight and strength, and went steadily downhill with more gastrointestinal symptoms than are indicated here. In spite of the fairly normal blood chemical findings I therefore made a tentative diagnosis of Addison's disease. The patient also had the benefit of stays at two sanatoriums, but did not improve. She never responded to psychotherapy.

DR. FULLER ALBRIGHT: The differential between Addison's disease and Simmonds's disease may be extremely difficult. Many of the manifestations of Simmonds's disease are due to secondary adrenal insufficiency. I saw this patient and came to the same conclusion that Dr. Ludwig came to, for the same reasons. There was perhaps one fallacy in our reasoning, though, which I have thought of since. Both he and I put emphasis on the fact that there was a negative test for follicle-stimulating hormone in the urine after the menopause. Since this test is normally positive after the menopause, the inference was that there was some deficiency of the pituitary gland. I am not sure, however, that you would get a positive test for follicle-stimulating hormone in a patient with Addison's disease and malnutrition after the menopause. The latter in itself inhibits the pituitary gland.

DR. J. H. MEANS: A great many points in this case have interested the members of the Thyroid Clinic. I agree with Dr. Ludwig that this woman had sufficient evidence to make a diagnosis of hypofunction of the anterior lobe, which in turn brings about a certain degree of hypothyroidism, hypogonadism and hypocortinism, probably all secondary to the anterior-lobe dysfunction. I should like to mention that Richardson² pointed out the resemblance of anorexia nervosa and Simmonds's cachexia. I think that the pituitary gland, though not actually diseased, may underfunction because of malnutrition. It is very difficult to say which is the cause in any given patient.

Another point that deserves comment is the statement that the patient received 12 gr. of thyroid. That is an excessive dose. Either it was not absorbed or else she did not get it, because such a dose ought to make her desperately ill. We have had several cases.

For example, one was that of a woman who years ago had had toxic goiter and had made a good recovery under x-ray treatment. Some years later she came in with symptoms of fatigue and showed a low basal metabolic rate. She improved markedly on small doses of thyroid. A number of years after that she was seen for a third time with similar symptoms. Thyroid was again ordered. After taking it for a short while she went into a state of collapse and was brought into the hospital. Study disclosed that she was in a state analogous to the crises in Addison's disease. Indeed, it turned out that she had Addison's disease and that the thyroid treatment had thrown her into the crisis. She was rescued by means of salt and cortin, but later at home—not having followed directions—she went into a second crisis and died.

We also had a woman of twenty-four who was sent into the hospital with a diagnosis of myxedema, in which we concurred. She was placed on thyroid, but in a few days went into a crisis similar to that of the patient just mentioned, from which she too was successfully rescued by salt and cortin. Our conclusion in this case was that she had a pituitary type of myxedema, secondary to anterior-lobe dysfunction, and although thyroid benefited the secondary hypothyroidism, it broke down the adrenocortical function and precipitated a crisis.

When one sees a patient with myxedema who is responding badly to thyroid, one should consider the possibility of anterior-lobe hypofunction. Such people do not tolerate thyroid well until they are protected against hypofunction of other glands by suitable substitution therapy.

The story that 12 gr. of thyroid was borne by the patient is a very puzzling fact; that is to say, if it is a fact.

DR. PALMER: That happened before I saw her. She improved greatly when she was taking thyroid for four or five months.

DR. TRACY B. MALLORY: I think there must have been a mistake in the recording of the dosage.

CLINICAL DIAGNOSES

Simmonds's disease?
Cystitis.

DR. LUDWIG'S DIAGNOSES

Hypofunction of anterior lobe of pituitary gland.
Urinary infection.

ANATOMICAL DIAGNOSES

Tuberculosis of the adrenal glands (Addison's disease?).
Atrophy of the anterior lobe of the pituitary gland, thyroid gland, parathyroid glands and ovaries (Simmonds's disease).
Cholelithiasis.
Salpingitis, chronic, left.

PATHOLOGICAL DISCUSSION

DR. MALLORY: At autopsy we thought we were going to have difficulty in confirming the diagnosis of Simmonds's disease, because we found both adrenal glands were caseous and it seemed as if we must be dealing with Addison's disease. However, on further investigation, the thyroid gland weighed only $3\frac{1}{2}$ gm. and the pituitary gland was composed mostly of posterior lobe. Shrunken, atrophied and scarred, the anterior lobe showed almost complete absence of basophilic cells, so I think there is no doubt that it really was Simmonds's disease. Outside of the endocrine system the only findings were terminal pyelonephritis,—which I do not think was very important,—chronic, non-tuberculous salpingitis and cholelithiasis.

DR. JOHN H. TALBOTT: How much normal cortical material remained?

DR. MALLORY: Roughly one tenth.

DR. TALBOTT: We have the impression that to produce typical Addison's disease the cortical tissue must be reduced to a very low percentage of normal and that some of these patients can carry on with only one fifth or one tenth of the usual amount of cortex.

DR. MALLORY: I think I have seen adrenals with about this amount of cortical tissue left in patients who did not have Addison's disease.

DR. MEANS: What do you think the sequence of events was?

DR. MALLORY: I cannot tie them together. I do not believe the lesion in the pituitary gland was tuberculous. There was nothing to suggest it.

DR. ALBRIGHT: You do not believe she had Addison's disease?

DR. MALLORY: I do not, although I cannot be dogmatic.

DR. TALBOTT: I did not see this patient at any time during her illness but remember having discussed the diagnosis with Dr. Palmer when she first came under his care. There were many points

in the history, the physical findings and laboratory data that suggested adrenal insufficiency. The subsequent course under his care confirmed this presumptive diagnosis. Absence of pigmentation was against a diagnosis of primary adrenal insufficiency, that is, Addison's disease, and in my opinion was consistent with adrenal insufficiency secondary to pituitary hypofunction. Up to the time of necropsy, this explanation seemed most reasonable. The findings of caseous adrenal glands in addition to pituitary and thyroid atrophy were most unexpected. This is my first encounter with such a combination. My interpretation of the case in the light of these findings would be primary adrenal insufficiency from tuberculous adrenal glands, secondary pituitary atrophy, and subsequently thyroid atrophy. With this interpretation, the pathologic processes could account for the whole clinical picture in logical sequence. The alternative explanation, that is, pituitary hypofunction and coincidental caseous adrenal glands, seems less likely.

REFERENCES

1. Simmonds, M. Ueber Kachexie hypophysären Ursprungs. *Deutsche med. Wochenschr.* 42:190, 1916
2. Richardson, H. B. Simmonds' disease and anorexia nervosa. *Tr. A. Am. Physicians* 52:141-145, 1937.

CASE 26412

PRESENTATION OF CASE

A thirty-one-year-old Swedish housewife entered the hospital complaining of fever and generalized aches and pains of ten months' duration.

At eighteen years of age, during a physical examination for life insurance, the patient was told that she had a heart murmur. This was not considered serious enough to bar her from obtaining a policy. Ten months before admission she noticed a constant dull ache in the lower three or four ribs of both sides of the chest, which was not related to respiration. In addition there was a constant ache in the lower thoracic vertebrae, which was not related to movement or position. These symptoms were accompanied by malaise, anorexia and loss of weight. A month passed, and she finally saw her physician who made a diagnosis of rheumatic fever. He kept her in bed for the next ten weeks and prescribed sodium salicylate tablets, and oil of wintergreen to the affected parts. The pain was relieved immediately, but she still suffered from anorexia and general malaise, lost 10 pounds in weight and ran a fever of 99 to 100°F. for nine weeks. For the next few months she felt fairly well, but fatigued easily and frequently noticed that her heart palpated and that she was dyspneic on climbing stairs.

From time to time her heart "skipped" a beat, and she had frequent night sweats. Ten weeks prior to entry she "caught cold" and had frequent chills, a temperature of 102°F. and a nonproductive cough; her ribs again became tender. She was given salicylates by her physician; the rib pain immediately disappeared, but the fever remained. Salicylates were increased to the point of emesis with no effect on the temperature, so they were discontinued for four days and then reinstituted in small doses and continued until two weeks before entry. The patient was then given 5 gr. of sulfanilamide five times a day for five days, with no beneficial results. During these five days the patient noticed a pain in the lower left chest in the region of the tenth and eleventh ribs; she described it as a "grating" sensation, increased by breathing and coughing, which frequently forced her to catch her breath.

Although joint pain had been absent, transient soreness and tenderness had occurred in the arms, fingertips and legs. About one month before entry a small subcutaneous lump appeared over the second left chondrosternal junction, which remained for about four days and then disappeared. Her physician said that this was a rheumatic nodule. She had had amenorrhea for the past two months. An Aschheim-Zondek test was negative.

At the age of two years the patient had had "malaria fever," according to her physician, and at ten, severe "flu," with epistaxis which lasted three weeks. She had also had the usual childhood diseases.

The family history was essentially non-contributory. The patient's husband and two children were alive and well.

Physical examination showed a well-developed and well-nourished woman, flushed but not in acute distress. A diffuse, regular, heaving impulse was seen over the precordium, and the apex of the heart was felt in the fifth interspace 10.5 cm. to the left of the midline. A systolic thrill was just palpable at the apex. A loud blowing systolic murmur was heard over the entire left chest. It was loudest at the apex and transmitted into the axilla and left back. The blood pressure was 136 systolic, 62 diastolic. The circumpatellar tissues of the left knee joint were slightly thickened, but there was no crepitation or restriction of movement.

The temperature was 99.6°F., the pulse 132 and the respirations 22.

Examination of the blood revealed a red-cell count of 4,490,000 with a hemoglobin of 74 per cent, and a white-cell count of 14,250 with 78 per cent polymorphonuclears. The urine showed a + test for albumin, an occasional red blood cell, 8 to 12 white blood cells and an occasional granu-

lar cast per high-power field and no bacterial growth. A blood Hinton test was negative.

X-ray films of the chest showed the transverse diameter of the heart to be 12.7 cm, with a chest diameter of 23.9 cm. The heart appeared slightly enlarged in the region of the left ventricle, and there was a questionable enlargement of the left auricle. The hilar shadows were not increased. Electrocardiographic recordings showed a normal rhythm with a rate of 105, a PR interval of 0.16 second and some somatic tremor.

The salicylates, which the patient had been getting almost continuously, were stopped; the temperature immediately rose, and stayed up even after salicylates were re-instituted. A blood culture at this time yielded 73 colonies of alpha hemolytic streptococci per cubic centimeter. Sulfapyridine therapy was started, but in nine days, when the blood level had reached 107 mg. per 100 cc, she developed crampy abdominal pain, hematuria and albuminuria, and the urine contained many sulfapyridine crystals. This treatment was stopped for a week and then continued in smaller doses, but with the same results. Sulfathiazole therapy for a week produced no beneficial results, but led to nausea and abdominal distress. The patient was then given three single days of continuous-drip neosarsphenamine therapy, spaced four days apart; the daily dose was 1 gm. For two weeks during and following this period the blood culture became negative, for the first and last time. Starting a week later the patient was given heparin for seven days, followed by three days of continuous-drip neosarsphenamine therapy and three days of neosarsphenamine and heparin therapy. The heparin was then continued for one week. She tolerated this intensive treatment well, but three days after the last administration of neosarsphenamine she developed paresthesia and numbness of both feet. These symptoms gradually became worse, and in two weeks a severe polyneuritis had developed, with wrist and toe drop, glove- and stocking anesthesia, absent reflexes, weakness of the muscles of the extremities and bladder hypotonia. An unsuccessful attempt had been made to prevent this complication by the use of thiamine hydrochloride. There were few embolic phenomena throughout her illness, but those that occurred were as follows: one week after admission small red points appeared in the palpebral conjunctiva of both lower eyelids, and a fingertip became sore, with no visible petechiae; eleven days later a tender indurated area could be felt in the left palm. About two months after admission the left ankle on its dorsal aspect became painful and tender, and movement of the joint was limited; the spleen could be felt for the first time.

With the establishment of the severe peripheral neuritis the patient pursued a gradual downhill course. Liver-function and kidney-function tests were normal on the completion of chemotherapy. During the last month of her illness the patient developed a cystitis, then diarrhea; hemorrhages appeared in the conjunctivas and fundi. About seventeen weeks after admission she complained of a sudden blurring of vision and a "funny feeling" in the back of the head. She lapsed into coma, and died ten hours later.

DIFFERENTIAL DIAGNOSIS

DR. EDWARD F. BLAND Usually in these conferences the discussor is expected to review the clinical data as given and to arrive at certain reasonable conclusions in regard to the cause of the patient's illness and death. The pathologist then checks us up. It seems to me that here we are not given much choice as to the differential diagnosis, for this record is almost a textbook recital of the classic manifestations of subacute bacterial endocarditis. In addition there are at least two groups of symptoms related more directly to the therapeutic agents employed than to the disease itself.

In the first place we probably have adequate evidence to suppose that minimal valvular disease preceded the appearance of the final infection. The mitral valve apparently had been scarred since childhood, and one or both of the two earlier illnesses may have been rheumatic fever. I am especially suspicious of the one labeled "flu," which lasted three weeks and was associated with nosebleeds. The patient did well thereafter and presumably had very little residual damage to the heart. We have no evidence of subsequent rheumatic activity, although this possibility must, or should, have been tentatively considered at the onset of the final illness, ten months before death, and before the results of the blood cultures were known. There are one or two points, however, even earlier in the illness that are rather strongly against rheumatic fever. The story of recurring chills is most unusual in rheumatic fever—chills sometimes occur but certainly they are extremely rare. The nodule for which a rheumatic origin was considered appeared rather quickly and disappeared in three or four days. Its transient nature, its location and the absence of similar nodules elsewhere are points against its rheumatic origin. I believe that it must have been an embolic phenomenon. Another point might legitimately be raised, as apparently it was, namely, the relief from salicylate therapy noted early in the record. We now know that the response to salicylate therapy is not quite so specific in rheumatic fever,

as opposed to that in other rheumatic and febrile diseases, as we had once thought. Therefore, in view of the very complete and convincing data here recorded, it is difficult to consider any possible diagnosis other than subacute bacterial endocarditis superimposed on minimal rheumatic scarring of the mitral valve.

The signs in the heart—the loud apical systolic murmur and the fullness of the left auricle in the x-ray films—indicate mitral regurgitation. This type of valvular deformity is very prone later to become the site of secondary bacterial infection. Aortic valves that regurgitate are also likely to be the site of bacterial endocarditis, as are almost all types of congenital defects in the heart. I think we must keep the bare possibility in mind that there was a slight congenital defect rather than rheumatic mitral regurgitation; but the prominence of the left auricle is fairly good evidence of previous scarring of the mitral valve, and the absence of emboli to the lungs negates a congenital septal defect or a patency of the ductus. Although only one of the blood cultures is specifically mentioned as being positive, it is said later that they were sterile only for a period of two weeks. We must therefore assume that there were many positive blood cultures for the same organism.

Next we come to the therapy. Whatever else one may say, I think we shall all agree that a very determined effort was made to combat the progress of this fatal infection. It is interesting to mention briefly a few of the renal complications following the use of the newer chemotherapeutic agents. Sulfapyridine crystals are not infrequently precipitated in the urine, particularly that in the renal pelvis or bladder, so that the symptoms therefrom are inclined to simulate "gravel" in the urine. The deposition of crystals of sulfathiazole, however, appears to take place in the renal tubules; hence the clinical picture is apt to resemble that of diffuse glomerulonephritis. In this case it is reasonable to assume that the gross hematuria and albuminuria were largely the result of sulfapyridine therapy.

Then we come to a second complication which I think was caused by the therapy and not by the disease itself, namely, the severe polyneuritis. I have not personally observed polyneuritis, nor can I find a record of such as a result of subacute bacterial endocarditis. Perhaps in patients as sick as this woman was it might rarely occur, but it has apparently not been described. On the other hand, polyneuritis is not unusual after the use of heavy metals. In this case I am inclined to attribute it to the presence of a heavy metal, namely, arsenic. Why was neoarsphenamine used? Arsenic has

been recommended for many years in one form or another as an agent to combat this infection. More recently a physician on the Pacific Coast has apparently had some success using it in a constant drip intravenously. I am not certain whether or not he has combined it with heparin. Perhaps he has, and I suspect that his results were in part responsible for the trial of the combined therapy in this case. It is not so stated, but I should like to ask whether this patient received sulfamethylthiazole prior to the appearance of the polyneuritis. We have seen peripheral neuritis after sulfamethylthiazole, but not after sulfanilamide, sulfapyridine or sulfathiazole. If the patient had received sulfamethylthiazole, it would add another agent that might have precipitated the polyneuritis. The spleen in the meantime became palpable. One wonders a little if the fingers also became clubbed, since that is about the only one of the classic signs of subacute bacterial endocarditis that is not specifically mentioned.

Finally, we come to the terminal few hours of this patient's life. Patients severely ill with this disease not infrequently lapse into coma before death. On the other hand, emboli arising in the heart and going to the brain, as well as to other parts of the body, are very common, in fact almost an essential feature of the disease. Following the institution of heparin therapy in this hospital there seemed to be an increase in the incidence of subarachnoid hemorrhage. But I have seen two patients with subarachnoid hemorrhage as a terminal event, neither of whom had received heparin. I consequently believe that in the beginning there was a slight overemphasis on heparin as a precipitating factor in cerebral hemorrhage. Perhaps, however, this still remains a real hazard. The fact that this patient did not develop paralysis is a little against a localized thrombosis or embolus—the head discomfort followed by dimness of vision and coma is more suggestive of subarachnoid hemorrhage. I suppose that, by the law of chance, cerebral infarction was the most likely, perhaps precipitating more extensive bleeding in the subarachnoid space. I conclude then, that this patient had chronic rheumatic heart disease, with scarring of the mitral valve, superimposed subacute bacterial endocarditis and a terminal subarachnoid hemorrhage.

DR. PAUL D. WHITE: It was during my term of general medical ward visits that this young woman entered the hospital. She looked surprisingly well for a person with a history of long illness, and there was not any clear indication at that time of subacute bacterial endocarditis, although, as Dr. Bland pointed out, her illness did not quite fit with

a diagnosis of rheumatic disease. I believe that she had acute rheumatic fever superimposed on chronic rheumatic heart disease with mitral valve deformity but that subacute bacterial endocarditis had to be ruled out. It was not ruled out but was ruled in very quickly by positive cultures—she was practically never free of these from the onset. It was still during the year of our experimental trials with chemotherapeutic agents, and we started off with sulfapyridine and then gave sulfathiazole. About two months before the patient died, there were three interesting comments. Dr. Mead wrote, "It looks as though we are licked, and I agreed with that. A few days later I wrote 'Review of the course of illness in the last few weeks makes me think that the chemotherapy, particularly with sulfapyridine, has had a somewhat retarding effect on the infection, but not enough in view of the toxic effects; for that reason I do not advise heparin.' Even then we realized that unless we got a favorable effect from the original drugs, sulfapyridine or an allied chemical, we could not expect much benefit from its combined use with heparin or from heparin alone. I also wrote 'Perhaps the new drug, sodium paranitrobenzoate, may be available for the patient before it is too late.' Was it given to this woman?"

DR SEDGWICK MEAD: No.

DR WHITE: It has not proved of any value in the few cases we have treated with it.

All subsequent attempts to stem the tide in this case were futile. During the next two months we did not use chemotherapy, but evidently neoarsphenamine was subsequently given, with toxic effect. I do not believe sulfamethylthiazole was used. She was, as I view her now, an unfavorable case almost from the start. There was little control of the infection, the temperature never came down to normal, and the blood was free from bacteria for only about two weeks.

A PHYSICIAN: That might have been due to the bacteriostatic effect of drugs.

DR WHITE: Only the cases that respond quickly and strikingly to initial treatment are likely to have a fair outlook. In such cases heparin as additional therapy may be worthwhile on theoretical grounds. We have noted very little harm from heparin, but definite untoward effects from such drugs as sulfapyridine and neoarsphenamine. Clinical work on the Pacific Coast in the use of neoarsphenamine and experimental work in vitro and in animals stimulated us to try the drug in a few patients, but we have had no luck with it. A few more favorable results have come from the combined use of sulfapyridine and heparin. Heparin was not responsible for the hemorrhage

in this case, because that drug was not being administered during the last few weeks of the patient's life. There is no prolonged effect on the clotting time by heparin after it has been withdrawn, and several other cases of subacute bacterial endocarditis not receiving heparin have had cerebral hemorrhages, as Dr. Bland has stated. Although heparin is likely to increase the probability of hemorrhage in the face of embolism, it is not commonly the cause of hemorrhage in these patients.

CLINICAL DIAGNOSES

Subacute bacterial endocarditis
Cerebral embolism

DR BLAND'S DIAGNOSES

Chronic rheumatic heart disease.
Mitral regurgitation
Subacute bacterial endocarditis.
Subarachnoid hemorrhage.

ANATOMICAL DIAGNOSES

Subacute bacterial endocarditis, mitral valve
Endocarditis, chronic rheumatic, mitral valve
Cerebral hemorrhage, with rupture into lateral ventricle and Sylvian fissure
Subarachnoid hemorrhage
Infarcts of spleen and kidney
Embolic nephritis.
Miliary infarcts of the myocardium

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: This case was inserted in these exercises to get some discussion of the more recent therapy used in cases of subacute bacterial endocarditis. The patient did have subacute bacterial endocarditis involving the mitral valve. The valve had been previously damaged, as evidenced by the thickened cusps and chordae tendineae, although there was no appreciable stenosis. The vegetations had extended down from the valve edge to the chordae tendineae and up on the auricular wall. There was no involvement of any of the other valves with either rheumatic infection or bacterial endocarditis. The patient also had infarcts of the spleen and kidney, and microscopic examination of the kidneys showed the usual finding of embolic nephritis. The myocardial sections contained many miliary infarcts, a finding that has been emphasized by Buchbinder and Saphir¹ as being a cause of heart failure in bacterial endocarditis. De Navasquez,² on the other hand, found these lesions in 95 per cent of his cases but believed there was no relation to heart failure.

DR. WHITE: Were there any renal calculi?

DR. CASTLEMAN: No.

The brain was quite interesting. There was a subarachnoid hemorrhage caused by the rupture of a large cerebral vessel into the Sylvian fissure. It had also ruptured into the lateral ventricle. I was under the impression that this hemorrhage was due to heparin, but it apparently had not been given to this patient for a long time.

DR. MEAD: She had not had heparin for the three weeks before death, and its effect wears off very quickly.

DR. CASTLEMAN: Perhaps it is only coincidental, but it is interesting to note that during the past year or so we have had about half a dozen cases of subacute bacterial endocarditis with massive cerebral hemorrhage—a finding that was very rare before the days of chemotherapy.

DR. WHITE: Two other facts should be men-

tioned. First, this patient with a relatively slight amount of disease in the mitral valve represents the type of case we encounter most commonly with this complicating disease. Secondly, it is just beginning to be realized that there is a wide range of strains of *Streptococcus viridans*, each one reacting differently to these various drugs; until more work is done in differentiating the reaction of the specific organism to the specific chemotherapeutic agent, we are not going to get very far in any particular case.

A PHYSICIAN: I should like to add that in a New York hospital where intensive arsenic therapy for syphilis has been carried out peripheral neuritis is a fairly frequent complication.

REFERENCES

1. Buchbinder, W. C., and Saphir, O.: Heart failure in subacute bacterial endocarditis. *Arch. Int. Med.* 64:336-347, 1939.
2. de Navasquez, S.: The incidence and pathogenesis of myocardial lesions in subacute bacterial endocarditis. *J. Path. & Bact.* 49:33-38, 1939.

The New England Journal of Medicine

Formerly the
Boston Medical and Surgical Journal
Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE
ON PUBLICATIONS

Official Organ of
THE MASSACHUSETTS MEDICAL SOCIETY
THE NEW HAMPSHIRE MEDICAL SOCIETY
THE VERMONT STATE MEDICAL SOCIETY

EDITORIAL BOARD

Joseph Garland M.D.	John P. Sutherland M.D.
William B. Breed M.D.	Stephen Rushmore M.D.
George R. Minot M.D.	Henry R. Vets. M.D.
Frank H. Lahey, M.D.	Robert M. Green M.D.
Sheldis Warren M.D.	Charles C. Lund M.D.
George L. Tobey, Jr., M.D.	John F. Fulton M.D.
C. Guy Lane M.D.	A. Warren Stevens M.D.
William A. Rogers M.D.	Dwight Hara M.D.

ASSOCIATE EDITORS

Thomas H. Lanman M.D.	Donald Munro M.D.
Henry Jackson Jr., M.D.	
Walter P. Bowers M.D.	EDITOR EMERITUS
Robert N. Nye, M.D.,	MANAGING EDITOR
Clara D. Davies	ASSISTANT EDITOR

SUBSCRIPTION TERMS \$6.00 per year in advance postage paid for the
United States Canada \$7.04 per year \$8.52 per year for all foreign coun-
tries belonging to the Postal Union

MATERIAL for early publication should be received not later than noon
on Saturday

THE JOURNAL does not hold itself responsible for statements made by any
correspondent

COMMUNICATIONS should be addressed to the *New England Journal of
Medicine*, 8 Fenway Boston Massachusetts

E PLURIBUS

Nor long ago a highly respected newspaper commented editorially on the hypothesis that America had at last completed its long retreat from illusionment.

A number of facts seem to give support to this statement. We no longer place reliance on our ocean boundaries or the continued effective goodwill of our neighbors. We are no longer confident in the practical value of our man power, untrained and unarmed; we have come suddenly to realize that soft gold is a base metal until the modern alchemist's touch has converted it into the tough steel of defensive armaments.

This conversion of our currency has commenced. We have voted vast appropriations for naval increase. So far as anyone knows we are building

planes on a constantly increasing scale of production. The American Medical Association has already started to organize the medical profession. We have almost enthusiastically supported Congress in a decision that is revolutionary and formerly undreamed of in this democracy—the passage of a conscription bill with the country officially at peace. We are almost pathetically eager that somehow our ramparts should be watched.

And yet with all this talk and activity one can sense beneath the surface a feeling of unreality; as if we truly believed it all to be an uncomfortable dream, from which we shall awaken to plod along again in our comfortable middle class fashion, concerned over our customary problems, but quite sure that we shall be getting up from the same bed in the same house for some time to come, with a hot breakfast ready on the table.

Despite our financial panics and our economic depressions, our worries over the price of veal chops and our personal, medical agitations concerning colored crosses and governmental interference with the practice of medicine, we have got along fairly well, and we do not want the affairs of the world to disturb us. We have reached that danger point in the history of a nation where an increasing gold reserve is balanced by a declining birth rate; where the accumulation of wealth may soon go hand in hand with the decay of man.

A common danger to which we shall eventually become fully awake, a retreat from illusionment which may soon be completed, a common cause in which our country will again become united may yet prove to be our moral, political and economic salvation. But regardless of what may happen on the face of the earth in the next few years, of one thing we can be certain. The world is going to be a tougher place in which to live than it has been for generations, and free men must be as tough to hold their places in it as they once were to win them.

Men now living will not again walk down the primrose path of the last few decades, and in this fact, too, may come salvation.

SURGICAL CATGUT U.S.P.

OVER eight years ago the deplorability of the lack of standards or regulations to ensure the sterility of surgical catgut was commented on editorially¹ in the *Journal*. At that time it was suggested that the National Institute of Health, the laboratory of the United States Public Health Service that so effectively guarantees the potency and sterility of biological products subjected to interstate distribution, was the logical agency for control. During the subsequent years, however, little occurred, other than a gradually, although slowly, increasing appreciation by hospitals and surgeons that the so-called "sterility" of such sutures, unless controlled by the method recommended by Meleney and Chatfield,² meant nothing and that the use of sutures other than those tested by this method was hazardous.

Some action has at last been taken, and the *Second Supplement* of the eleventh decennial revision of the *United States Pharmacopoeia* establishes standards for surgical catgut, the development of which was made possible through the establishment of the Sterile Products Advisory Board, with the co-operation of various interested parties. These include tests for sterility,—as recommended by Meleney and Chatfield, revised by Clock³ and used by Brewer,⁴—for tensile strength and for length and diameter. No test for absorption is presented, but it is specified that tanned catgut or that otherwise treated to resist digestion shall carry the notation "mild treatment," "medium treatment" or "prolonged treatment," depending on the duration of the procedure. These standards become official on January 1, 1941, and thereafter all catgut intended for surgical use must, according to the Food, Drug and Cosmetic Act, meet the requirements. Any product failing to conform must be labeled in such a way as to indicate in every respect the manner in which it differs.

The omission of a standard for absorption is regrettable but wise, for no test has yet been devised that serves as an adequate measure of this property. Tests for absorption in animals are not necessarily applicable to the results in human beings. The Advisory Board is favorably impressed

by in vitro tests using trypsin as the digestive solution,⁵ but there are various factors that must be controlled before this method will become a reliable test of absorption. This one property—so important in the reduction of the dangers due to hemorrhage or leakage and in the incidence of wound disruption—must, for the moment, remain unstandardized, other than for the previously mentioned requirement that the time of processing be specified. A forward step has been taken, however, and the surgeon can at least be assured of a sterile product of accurate length and size and of suitable tensile strength.

REFERENCES

- 1 Editorial Sterile surgical catgut. *New Eng. J. Med.* 207:375, 1932.
- 2 Meleney, F. L., and Chatfield, M.: The sterility of catgut in relation to hospital infections. *Surg., Gynec. & Obst.* 52:430-441, 1931.
- 3 Clock, R. O.: Bacteriologic testing of catgut sutures. *J. Lab. & Clin. Med.* 18:61-63, 1932. A reliable method for testing the sterility of catgut sutures. *Surg., Gynec. & Obst.* 61:769-793, 1935.
- 4 Brewer, J. H.: The present status of the sterility of catgut sutures on the American market. *J. A. M. A.* 108:722-727, 1937.
- 5 Kraissl, C. J., and Meleney, F. L.: A method for determining the time of catgut digestion in vitro. *Surg., Gynec. & Obst.* 59:161-164, 1934.

MEDICAL EPONYM

EHRlich's DIAZO REAGENT

"Ueber eine neue Harnprobe [A New Urine Test]" is the title of an article by Professor Paul Ehrlich (1854-1915) which appeared in the *Zeitschrift für Klinische Medizin* (5:285-288, 1882). A portion of the translation follows:

The diazo groups, which are produced by the reaction of nitric acid on the amido groups of the aromatic series, have the ability, as is well known, to combine with a large number of substances, particularly the mono-, di- and poly-phenols as well as the primary, secondary and tertiary mono- and di-amines of the aromatic series, with color formation.

This reaction . . . seemed susceptible of medical use. That is, it was to be expected that substances might be present in the secretions and excretions of the human body, but above all in the urine, which would give color reactions with the diazo groups. . . . Indeed my expectations have been confirmed, and these substances have given color reactions in the urine which seem by reason of their significance to be adapted to clinical and diagnostic use. . . .

The solution which I used is prepared as follows: I strongly acidify a moderate amount of water, about 500 cc., with pure nitric acid (30-50 cc.) and add to this enough sulfanilic acid, which is rather difficultly soluble, so that the excess sinks to the bottom. A few granules of sodium nitrite are now dissolved in water in a test tube, and this solution is gradually added, with shaking, to the first. The above-described reagent retains its efficacy, particularly if the weather is not too warm, for some time; it remains useful for two to three days in summer, or as much as five days in winter.

R. W. B.

OBITUARY

AUGUSTUS THORNDIKE

1863-1940

Dr. Augustus Thorndike died suddenly on August 23, 1940, at his summer home in Bar Harbor, Maine, at the age of seventy-seven years.

His wife, the former Alice Amory, of Boston, whom he married in 1892, died two years ago. They had five children, who survive him: Mrs. Lyncham Crocker, Mrs. Alexis Sommarina, Dr. Augustus Thorndike, Jr., Charles Thorndike and Robert Amory Thorndike.

He was born in Paris, but his education was received in this country. After graduating from Harvard College in 1884 and from Harvard Medical School in 1888, he served as intern on the Surgical Service at the Massachusetts General Hospital, at the Boston Lying-in Hospital and at the House of the Good Samaritan.

From the beginning of his practice Dr. Thorndike was interested in orthopedic surgery, and until his retirement in 1918 he played an active part in this department of medicine in New England. He was a member of the staffs of the Children's Hospital and of the House of the Good Samaritan, and in addition was associated at times with the Boston Dispensary in the Orthopedic Department and also at St. Luke's Home for Convalescents. At that time a large proportion of the cases were tuberculous, and, since the hospital equipment was much more limited than at present, they required a great deal of careful personal attention from those who were in direct charge. Dr. Thorndike's capacity for conscientious care and the great sympathy which characterized his attention to his patients were evidenced by the success which he had with these difficult cases. As visiting surgeon, he gave a great deal of his time to this work at the House of the Good Samaritan, which was then one of the few institutions providing treatment for such cases, and during all his professional career he was an active member of the staff of the Boston Children's Hospital where his work was characterized by the same conscientious care and sympathy. He was particularly concerned with the problem of the crippled child, in relation not only to medical care but to education and occupational training. He was one of the incorporators of the Boston Industrial School for Crippled Children and was actively interested in the establishment of the State Hospital School for Children at Canton.

He was an active member of many societies in and about his home,—the Massachusetts Medical

Society, the Boston Medical Benevolent Society and the Society of Medical Sciences,—and he was also interested in the Boston Medical Library. Dr. Thorndike was a member of the American Medical Association. He was also a member of the American Orthopedic Association, to which he was elected in 1893, and served as its president for the year 1909-1910. He always took an active interest in this association, and the welcome accorded him at the meetings was evidence of the high esteem in which he was held.

Dr. Thorndike was generous in his estimate of his associates, never sparing in his efforts to help, and he gave freely of himself. He had the faculty of bringing out the best in those with whom he worked. He had definite and strong convictions but was always kindly and tolerant toward the opinions of others even when differing from them.

MASSACHUSETTS MEDICAL SOCIETY

THE ONE HUNDRED
AND SIXTIETH ANNIVERSARY

The exercises of the one hundred and sixtieth annual meeting of the Massachusetts Medical Society will be held in the Copley-Plaza Hotel, Boston, on May 21 and 22, 1941.

SECTION OF OBSTETRICS
AND GYNECOLOGY*

RAYMOND S. TITUS, M.D., *Secretary*
330 Dartmouth Street
Boston

DIABETES AND PREGNANCY IN
THE PRE-INSULIN ERA

Mrs. J. R., a twenty-nine-year-old primipara, was first seen on September 15, 1919. She was referred by her family physician because of sugar in the urine.

The family history was non-contributory. The patient's past history included asthma and pleurisy. Catamenia began at fourteen, were regular with a twenty-eight-day cycle and lasted four to five days. The last period began on March 27, making the expected date of confinement January 4, 1920.

Physical examination revealed a thin woman. The heart was not enlarged; there was a systolic murmur at the base. The lungs were clear and resonant; there were no rales. The blood pressure

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

was 120 systolic. Abdominal palpation revealed a uterus enlarged to the size of a four and half months' pregnancy. Vaginal examination revealed a long cervix. There was considerable sugar in the urine, and the patient was referred to a specialist in diabetes.

On September 16 the patient entered the hospital for treatment. On entrance the urine contained 5.3 per cent sugar. The weight was 99 pounds. She was placed on a diet of 50 gm. of carbohydrate, 75 gm. of fat and 46 gm. of protein. The total caloric intake was raised from 700 to 1100. On this diet the amount of sugar in the urine was reduced to a fraction. Fasting blood-sugar determinations were normal—100, 160 and 100 mg. per 100 cc. The blood-cholesterol level was 167 mg. per 100 cc. There was no albumin in the urine. The blood pressure was 110 systolic, 75 diastolic. A blood Hinton test was negative.

The patient left the hospital on October 3 and was seen in the office on November 1 and again on December 15. On the diet containing approximately 1100 calories the amount of sugar in the urine varied from 0.2 to 0.4 per cent. The blood sugar remained normal. At the time of the latter visit the weight was 120 pounds, a gain of over 20 pounds. She had a considerable amount of edema, but the urine contained only the slightest possible trace of albumin. The blood pressure was 135 systolic, 80 diastolic.

On December 16, the day following the office visit, labor started spontaneously. At this time the patient was approximately thirty-seven to thirty-eight weeks pregnant. She was admitted to the hospital. Labor was simple, and a low-forceps delivery under gas was readily accomplished. The baby was very thin, long and decidedly undernourished, weighing 4 pounds, 15 ounces. The mother made an uneventful convalescence. The baby did well and was discharged well.

While in the hospital the diet, at first, consisted of 62 gm. of carbohydrate, 54 gm. of fat and 64 gm. of protein. This was subsequently raised to 79 gm. of carbohydrate, 107 gm. of fat and 83 gm. of protein, a caloric intake approaching 1600 calories. Upon the latter diet the blood sugar was normal, and the urine sugar-free; the blood pressure was 120 systolic, 80 diastolic. Her weight at the time of discharge from the hospital was 86 pounds. A sugar tolerance test done at this time gave the following values: fasting, 80 mg.; one hour, 160 mg.; two hours, 170 mg. per 100 cc.

On October 17, 1920, the patient was seen by the medical consultant. She had not tested the urine since the previous February. She had had amenorrhea since delivery. The weight was 82

pounds, and she had been eating what she chose. The urine showed 1 per cent sugar, and the blood-sugar level was 260 mg. per 100 cc. She died in diabetic coma a year and a half later.

Comment. This case is illustrative of diabetes in the pre-insulin era. Whether the diabetes existed before pregnancy or developed during pregnancy is unknown. The patient was kept alive on a diet that was barely sustaining, resulting in a very much undernourished infant in contrast to the overnourished diabetic babies seen so frequently at that time and still seen. Like so many other diabetic patients this woman did not go to term but started labor two to three weeks prematurely. Pregnancy undoubtedly did her no good, and even if she had been more conscientious about her diet, the final outcome would probably have been the same.

In the pre-insulin era, diabetic patients who were fortunate enough to become pregnant too frequently delivered themselves of overnourished, macerated infants, and only those whose disease was of moderate severity and who were kept on practically a starvation diet were fortunate enough to give birth to living children. As will be illustrated in subsequent cases, the administration of insulin has entirely changed this picture.

POSTGRADUATE EXTENSION COURSES

The postgraduate extension courses for the academic year 1940-41 will be given in three divisions as follows:

FALL	DISTRICT	PLACE
	Barnstable	Hyannis
	Bristol North	Taunton
	Bristol South	New Bedford
	Essex North	Lawrence
	Essex South	Salem
	Middlesex North	Lowell
	Plymouth	Brockton
WINTER		
	Middlesex East	Melrose
	Middlesex South	Cambridge
	Norfolk	Norwood
	Norfolk South	Quincy
	Suffolk	Boston
	Worcester	Worcester
SPRING		
	Berkshire	Pittsfield
	Bristol South	Fall River
	Franklin	Greenfield
	Hampden	Holyoke
	Hampshire	Springfield
	Worcester	Northampton
	Worcester North	Milford
		Fitchburg

all sessions begin this month; details of the program are listed below. Programs for the winter and spring courses will be printed prior to opening sessions. Printed programs with confirmation will be mailed to every registered physician before the courses begin. These courses are sponsored by the Massachusetts Medical Society in co-operation with the Massachusetts Department of Public Health, the United States Public Health Service and the Federal Children's Bureau. Registration is free to all legally registered physicians of the Commonwealth. For further information the district chairman of postgraduate instruction should be consulted.

The programs for the fall sessions are as follows:

BARNSTABLE DISTRICT: HYANNIS

SUBJECT	DATE
Recent Advances in Medical Therapeutics: Sedatives; analgesics; cathartics; sulfanilamide compounds; dangerous drugs	October 27
Dermatitis and Eczema (see below)	November 3
Chemotherapy in the Treatment of Gonococcal Infection	November 10
Pediatric Case Discussions	November 17
Technic and Treatment of Primary, Secondary and Tertiary Syphilis	November 24
Operative Obstetrics: Indications and technic	December 1
Management of Abdominal Distention	December 8
Obstetric Complications, with Case Histories and Clinical Problems	December 15
Meetings to be held at the Cape Cod Hospital, Hyannis, Sundays, at 4:00 p.m.	

Donald E. Higgins, M.D., *Chairman*
Main Street, Cotuit

BRISTOL NORTH DISTRICT: TAUNTON

SUBJECT	DATE
Infections of the Hands and Feet	October 24
Obstetric Complications, with Case Histories and Clinical Problems	October 31
Pediatric Case Discussions	November 7
Acute Abdominal Pain: Its interpretation and management	November 14
Therapeutic Uses of Preparations of Endocrine Glands: Thyroid gland, pituitary gland, ovary, testis and adrenal cortex	November 21
Dermatitis and Eczema (see below)	December 5
Technic and Treatment of Primary, Secondary and Tertiary Syphilis	December 12
Gonococcal Infections in the Armed Forces and the Civilian Population	December 19
Meetings to be held at the Morton Hospital, Taunton, Thursdays, at 4:00 p.m.	

Lester E. Butler, M.D., *Chairman*
148 High Street, Taunton

Note: Because of the holiday, the course will be omitted November 28.

BRISTOL SOUTH DISTRICT: NEW BEDFORD

SUBJECT	DATE
Gonococcal Infections in the Armed Forces and the Civilian Population	October 25

Diagnosis and Treatment of Minor Lesions of Rectum and Anus	November 1
The Clinical Recognition of the Types of Jaundice and Recent Advances in Their Treatment	November 8
The Treatment of Varicose Veins	November 15
Pediatrics (subject to be announced)	November 22
Acute Abdominal Pain: Its interpretation and management	November 29
Technic and Treatment of Primary, Secondary and Tertiary Syphilis	December 6
Operative Obstetrics: Indications and technic	December 13

Meetings to be held at St. Luke's Hospital, New Bedford, Fridays, at 4:00 p.m.

Robert H. Goodwin, M.D., *Chairman*
286 Pleasant Street, New Bedford

ESSEX NORTH DISTRICT: LAWRENCE

SUBJECT	DATE
Diagnosis, Treatment and Prognosis of Central-Nervous System Syphilis.	October 25
Therapeutic Uses of Preparations of Endocrine Glands: Thyroid gland, pituitary gland, ovary, testis and adrenal cortex	November 1
Management of Abdominal Distention	November 8
Obstetric Complications, with Case Histories and Clinical Problems	November 15
Infections of the Hands and Feet	November 22
Pediatric Case Discussions	November 29
Chemotherapy in the Treatment of Gonococcal Infection.	December 6
Dermatitis and Eczema (see below)	December 13

Meetings to be held at the Clover Hill Hospital, 161 Berkeley Street, Lawrence, Fridays, at 4:30 p.m.

John Parr, M.D., *Chairman*
7 Hampshire Street, Methuen

ESSEX SOUTH DISTRICT: SALEM

SUBJECT	DATE
Operative Obstetrics: Indications and technic	October 22
Pediatric Case Discussions	October 29
Technic and Treatment of Primary, Secondary and Tertiary Syphilis.	November 5
Nutritional Deficiencies and the Uses of Preparations of Vitamins	November 12
Diagnosis and Treatment of Minor Lesions of Rectum and Anus	November 19
Chemotherapy in the Treatment of Gonococcal Infection	November 26
Management of Abdominal Distention	December 3
Recent Advances in Medical Therapeutics: Sedatives; analgesics; cathartics; sulfanilamide compounds; dangerous drugs	December 10

Meetings to be held in the Conference Room, Salem Hospital, Tuesdays, at 4:00 p.m.

J. Robert Shaughnessy, M.D., *Chairman*
24½ Winter Street, Salem

MIDDLESEX NORTH DISTRICT: LOWELL

SUBJECT	DATE
Diagnosis and Treatment of Minor Lesions of Rectum and Anus	October 25

Chemotherapy in the Treatment of Gonococcal Infection.	November 1
Problems in Bronchoscopy.	November 8
Recent Advances in Medical Therapeutics: Sedatives; analgesics; cathartics; sulfanilamide compounds; dangerous drugs	November 15
Operative Obstetrics: Indications and technic	November 22
Technic and Treatment of Primary, Secondary and Tertiary Syphilis	November 29
Pediatric Case Discussions	December 6
The Treatment of Varicose Veins	December 13

Meetings to be held at St. John's Hospital, Lowell, Fridays, at 5:00 p.m.

William S. Lawler, M.D., *Chairman*
53 Central Street, Lowell

PLYMOUTH DISTRICT: BROCKTON

SUBJECT	DATE
Nutritional Deficiencies and the Uses of Preparations of Vitamins	October 22
The Treatment of Varicose Veins	October 29
Chemotherapy in the Treatment of Gonococcal Infection.	November 5
Pediatric Case Discussions	November 12
Technic and Treatment of Primary, Secondary and Tertiary Syphilis	November 19
Hemorrhage in Pregnancy, Labor and the Puerperium: Its diagnosis and treatment	November 26
Recent Advances in Medical Therapeutics: Sedatives; analgesics; cathartics; sulfanilamide compounds; dangerous drugs	December 3
Diagnosis and Treatment of Minor Lesions of Rectum and Anus	December 10

Meetings to be held in the Nurses' Home of the Brockton Hospital, Tuesdays, at 4:30 p.m.

Walter H. Pulsifer, M.D., *Chairman*
26 Park Avenue, Whitman

The following questions will be discussed in the course on dermatitis and eczema:

- Is there such a thing as eczema?
- Is allergy fact or fiction?
- Are skin tests of value in dermatology?
- Are fungous infections (athlete's foot) as prevalent as we are led to believe?
- With the diagnosis made, what should be the treatment of common cutaneous eruptions?

DEATHS

HARMER — TORR W. HARMER, M.D., of Winchester, died October 2. He was in his sixtieth year.

Born in Somerville, he attended the local schools and Harvard College, receiving his degree from Harvard Medical School in 1907. He served as surgical house officer at the Massachusetts General Hospital, house physician at the Boston Lying-in Hospital and assistant surgeon at the Infants' Hospital and the Children's Hospital. Dr. Harmer was a consulting surgeon at the Massachu-

setts Eye and Ear Infirmary and at the Somerville, Winchester, Symmes Arlington and Waltham hospitals.

He was a member of the staff of the Harvard Medical School for many years, having been assistant in surgery and instructor in anatomy. At the time of his death he held the position of instructor in anatomy.

A fellow of the Massachusetts Medical Society and the American Medical Association, he was also a member of the American Association for the Surgery of Trauma, the American College of Surgeons, the American Board of Surgery and the New England Surgical Society. His affiliations included the Aesculapian and Lancet clubs, of Boston.

His widow, a daughter, a son and a sister survive him.

JACKSON — HENRY JACKSON, M.D., of Chestnut Hill, died October 4. He was in his eighty-third year.

Born in Boston he attended the Hopkinson School and Harvard College and received his degree from Harvard Medical School in 1884. He served his internship at the Massachusetts General Hospital, after which he spent a year in Europe, studying at Vienna. From 1886 to 1916 he was a staff member of the Boston City Hospital, eventually becoming physician-in-chief. Dr. Jackson also served as an instructor in clinical medicine at the Harvard Medical School.

He was a member of the Massachusetts Medical Society, the American Medical Association and the Association of American Physicians.

His daughter, Mrs. Kennard Winsor, and a son, Dr. Henry Jackson, Jr., survive him.

SWAN — LAURENCE C. SWAN, M.D., of Beverly, died October 2. He was in his sixtieth year.

Born in Stoughton, he attended Dartmouth College and received his degree from Harvard Medical School in 1907. Shortly after graduation he settled in Beverly, where he practiced for over thirty-one years. Dr. Swan was a fellow of the Massachusetts Medical Society and the American Medical Association.

His widow, a daughter, a son and a brother survive him.

VILLONE — ANTHONY J. VILLONE, M.D., of Quincy, died October 6. He was in his fiftieth year.

Dr. Villone attended Fordham University and received his degree from Tufts College Medical School in 1918. He then enlisted in the Medical Corps of the United States Navy, and was a retired lieutenant. Dr. Villone was a member of the Massachusetts Medical Society and the American Medical Association.

His widow, parents, two sisters and two brothers survive him.

CORRESPONDENCE

RESULTS OF MARCH, 1940, BOARD EXAMINATIONS

To the Editor: I am enclosing a statement of the results of the March, 1940, examination conducted by the Board of Registration in Medicine.

STEPHEN RUSHMORE, M.D., *Secretary*.
State House, Boston

SCHOOL	FIRST TIME		SECOND OR THIRD TIMES		FOURTH OR MORE TIMES		TOTAL		TOTAL APPLICANTS
	PASSED	FAILED	PASSED	FAILED	PASSED	FAILED	PASSED	FAILED	
Boston University School of Medicine*	2						2		2
College of Physicians and Surgeons (Boston)	1		2	10	1		3	13	16
Harvard Medical School*	6						6		6
Massachusetts College of Osteopathy†	1		7	8			8	8	16
Middlesex University School of Medicine	2	7	18	21	3	6	23	34	57
Tufts College Medical School*	9						9		9
Taylor University College of Medicine*			1				1		1
Chicago College of Osteopathy†				1				1	1
Chicago Medical School	1						1		1
College of Medical Evangelists*			1				1		1
George Washington University School of Medicine*	2						2		2
Georgetown University School of Medicine*			1				1		1
Hahnemann Medical College and Hospital of Philadelphia*	1						1		1
Indiana University School of Medicine*	1						1		1
Jefferson Medical College of Philadelphia*	1						1		1
Johns Hopkins University School of Medicine*	2						2		2
Kansas City University of Physicians and Surgeons		1	2	7	1	5	3	13	16
Kirkville College of Osteopathy and Surgery†			4	1		2	4	3	7
Mid West Medical College			3	1	2	3	5	4	9
Philadelphia College of Osteopathy†			1	1	2		3	1	4
St. Louis College of Physicians and Surgeons				1				1	1
Tulane University of Louisiana School of Medicine*	1						1		1
University of Cincinnati College of Medicine*	1						1		1
University of Illinois College of Medicine*	1						1		1
University of Minnesota Medical School*	1						1		1
University of Tennessee College of Medicine*	1						1		1
University of Rochester School of Medicine*	1						1		1
University of Virginia Department of Medicine*	1	1					1	1	2
University of Wisconsin Medical School*	1						1		1
Albert University*	1						1		1
Elizabeth University*			1				1		1
McGill University*	3						3		3
Royal University Hungary*	1						1		1
University of Basle*		1						1	1
University of Berlin*	2			1			2	1	3
University of Bern*	2						2		2
University of Bologna*	1		1				2		2
University of Breslau*	5						5		5
University of Edinburgh*			1				1		1
University of Frankfurt*	2						2		2
University of Freiburg*	1						1		1
University of Hamburg*				1				1	1
University of Heidelberg*	2						2		2
University of Koenigsberg*	1		1				2		2
University of Lausanne*	1				1		2		2
University of Leipzig*	1						1		1
University of Milan*	3						3		3
University of Montreal*	1						1		1
University of Munich*	4						4		4
University of Naples*			1	1			1	1	2
University of Paris*			1				1		1
University of Prague*	3		1				4		4
University of Tartu (Estonia)*					1			1	1
University of Vienna*	21	1	1				22	1	23
	92	11	48	54	9	20	149	85	234

*Approved schools
†Osteopathic schools

Approved schools	87	3 ^b	11	3 ^b	1	1 ^b	99	7 ^b	106
Non approved schools	4	8	25	40	6	17	35	65	100
Osteopathic schools	1		12	11	2	2	15	13	28
	92	11	48	54	9	20	149	85	234

^bThe exponents represent graduates of European schools

COMMITTEE FOR THE DEFENSE OF MEDICAL RIGHTS

To the Editor: The Executive Committee of the Committee for the Defense of Medical Rights has issued a statement in support of an initiative petition to amend the Massachusetts laws relating to the prevention of pregnancy. The petition, which would allow physicians to provide medical contraceptive information and care to married persons for the protection of life or health, and which was filed with the Secretary of State on September 4, was signed by the following citizens of Massachusetts: Karl T. Compton, Sarah T. Curwood, Robert G. Dodge, Frederick M. Eliot, Nathaniel W. Faxon, M.D., Frederick C. Irving, M.D., William R. Manchester, Mary Pratt Potter, John Rock, M.D., and Curtis C. Tripp, M.D.

In the initiative petition the Legislature is asked to amend Sections 20 and 21 of Chapter 272 of the General Laws by adding at the end thereof the following:

The provisions of this section and of section twenty which relate to the prevention of pregnancy and the prevention of conception shall not apply to treatment or prescription given to married persons for protection of life or health by or under the direction of physicians registered in accordance with the provisions of Chapter 112; nor to teaching in chartered medical schools; nor to publication or sale of medical treatises or journals.

The statement issued by the Executive Committee reads as follows:

The initiative petition proposed is for a bill to ensure to physicians the right to protect the life, health and reason of married persons when these might be endangered by pregnancy. It is designed to prevent the legal interference with this phase of the practice of medicine, which has only recently resulted from the enforcement of an old Massachusetts statute.

The principle of legal freedom for physicians to provide contraceptive medical care to married women whose physical or mental condition would suffer by pregnancy or who could be expected to produce only seriously defective individuals has been approved by the American Medical Association, and by many other medical and religious bodies.

Support of this petition does not imply support of either the methods or philosophy of "birth control." It means only support of the principle of freedom in the licensed teaching and practice of medicine.

The initiative petition is so designed as to protect marital security and to bring under licensed control the present, widespread bootleg traffic in contraceptive information and material.

Under the constitutional procedure laid down for the presentation of initiative petitions to the Legislature, 20,000 signatures of registered Massachusetts voters, certified by the registrars of voters of the cities and towns of their respective residences, must be appended to this petition and filed with the Secretary of State by December 4 of this year. It is understood that 40,000 signatures will actually be sought by November 8, in order to be assured of fulfilling the legal requirements, and in order to have time for certification and checking of signatures before the December 4 deadline.

The Secretary of State will transmit the initiative petition to the 1941 Legislature, which convenes in January. It will then be referred to the proper committee for public hearings, and reported to the Legislature, where a recorded vote is required by law on or before the first

Wednesday in June. If the Legislature does not enact the proposed amendment, 5000 additional signatures of registered voters may be obtained between the first Wednesday in June and the first Wednesday in August, to be filed with the Secretary of State by the latter date. The question will then be submitted to the voters as a referendum in November, 1942.

Physicians who wish to aid in obtaining signatures to the initiative petition may obtain blanks by getting in touch with Somers H. Sturgis, M.D., Secretary, Committee for the Defense of Medical Rights, 270 Commonwealth Avenue, Boston.

WILLIAM H. ROBEX, M.D., *President,*
Executive Committee,

Committee for the Defense of Medical Rights.

270 Commonwealth Avenue,
Boston.

NOTICES

BOSTON DOCTORS' SYMPHONY ORCHESTRA



The Boston Doctors' Symphony Orchestra will rehearse under Alexander Thiede, former concertmaster with the Cleveland Symphony Orchestra, every Thursday at 8:30 p.m. Those interested in becoming members should com-

municate with Dr. Julius Loman, Pelham Hall Hotel, Brookline (BEA 2430).

PETER BENT BRIGHAM HOSPITAL

Weekly clinicopathological conferences will be held in the amphitheater on Mondays from 12:15 to 1:15.

Weekly clinicoroentgenological conferences will be held every Tuesday in the amphitheater between 12:15 and 1:15.

SUFFOLK DISTRICT MEDICAL SOCIETY

The 1940-1941 program of the Suffolk District Medical Society contains certain innovations, the most important being a noon luncheon meeting. Three meetings, rather than five as in previous years, will be held. The fall meeting will be the stated meeting, the midwinter the scientific meeting and the spring the annual meeting.

PROGRAM

Stated Meeting. Wednesday, October 30. Hotel Somerset.

12:00 m. Luncheon for those members who indicate their desire to be present.

12:45 p.m. Business meeting.

1:00 p.m. "Lessons for Physicians and Surgeons from the Army and Navy." Speakers to be announced.

Scientific Meeting. Wednesday, January 29. Boston Medical Library.

8:15 p.m. "Sedatives, Hypnotics and Anesthetics." Speakers to be announced.

Annual Meeting. Wednesday, April 30. Boston Medical Library.

8:15 p.m. "Symposium on the Toxemias of Pregnancy." To be arranged by Dr. Raymond S. Titus.

MASSACHUSETTS MEMORIAL HOSPITALS

There will be a staff meeting of the Massachusetts Memorial Hospitals in the Evans Memorial Auditorium on Friday, October 25, at 8 15 p m Dr Chester S Keeter will be the chairman

PROGRAM

Current Concepts of the Pathologic Physiology of Hypertension Dr Robert W Wilkins Discussion by Drs Reginald H Smithwick and James P O'Hare
Roentgenologic Aspects of the Heart in Hypertension Dr George Levene Discussion by Dr Merrill Sosman

PETER BENT BRIGHAM HOSPITAL

A joint medical and surgical clinic at the Peter Bent Brigham Hospital will be held on Wednesday, October 16, from 2 to 4 p m Drs C S Burwell and H F Newton will speak on "Dyspnea and Cough" A clinicopathological conference, conducted by Dr Elliott C Cutler, will take place from 4 to 5 p m.

Physicians and students are cordially invited to attend

NEW ENGLAND PATHOLOGICAL SOCIETY

The next meeting of the New England Pathological Society will be held in the amphitheater (Vila Street) of the Boston Children's Hospital on Thursday evening October 17, at 8 15

PROGRAM

Macrogonitosisma Praecox Associated with Hypothalamic Tumors Dr Robert E Gross
Natural Vital Staining of Teeth of the New Born Dr Paul E Boyle
Marble Bones Dr Albert Frank
Schüller-Christian's Disease and Allied Disorders Dr Sidney Farber

An exhibit illustrating some of the research activities of the Department of Pathology of the Children's Hospital (Shattuck Street entrance), and specimens of interest selected from routine surgical and autopsy material will be on display, from 7 00 to 8 15 and again after the meeting

NEW ENGLAND WOMEN'S MEDICAL SOCIETY

The fall meeting of the New England Women's Medical Society will be held at the Myles Standish Hotel on Thursday, October 17, at 7 00 p m Dr Timothy Leary will speak, his subject being "Some Experiences of a Medical Examiner"

ST. PAUL'S CATHEDRAL

A special service will be held at St Paul's Cathedral, Tremont Street, Boston, on Sunday evening, October 20, at 7 00 Dr Nathan B Van Etten, president of the American Medical Association, will speak, the title of his address being "Medical Horizons" All doctors, nurses and medical students are cordially invited

NEW ENGLAND SOCIETY OF PHYSICAL MEDICINE

The regular monthly meeting of the New England Society of Physical Medicine will be held on Wednesday evening, October 16, at the Hotel Kenmore, Boston

The council will meet at 6 00, and an informal dinner will be held in the Empire Room at 6 30 At 8 00, Mr

Robert D Beaird, technical engineer of General Electric X-ray Corporation, Chicago, will speak on the subject, "Medical Electrophysics"

All members of the medical profession are cordially invited to attend

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING SUNDAY, OCTOBER 13

MONDAY OCTOBER 14

12 15-1 15 p m Clin copathological Conference Peter Bent Brigham Hospital amphitheater

TUESDAY OCTOBER 15

9-10 a m Steroid Hormone Excretion Rates Associated with Dysmenorrhea Drs N T Verthessen and R E Brownlee Joseph H Pratt Diagnostic Hospital

12 m The Diagnosis and Treatment of Pulmonary Bleeding Dr Mosca J Stone South End Medical Club Headquarters of the Boston Tuberculosis Association 554 Columbus Avenue Boston

12 15-1 15 p m Clin copathological conference Peter Bent Brigham Hospital amphitheater

WEDNESDAY OCTOBER 16

9-10 a m Hospital case presentation Dr S J Thannhauser Joseph H Pratt Diagnostic Hospital

12 m Clinicopathological conference Children's Hospital

2-4 p m Dyspnea and Cough Drs C S Burwell and H F Newton Joint medical and surgical clinic Peter Bent Brigham Hospital

8 p m Medical Electrophysics Mr Robert D Beaird New England Society of Physical Medicine Hotel Kenmore Boston

THURSDAY OCTOBER 17

9-10 a m Nephritic Clinic Dr R W Buck Joseph H Pratt Diagnostic Hospital

7 p m Some Experiences of a Medical Examiner Dr Timothy Leary New England Women's Medical Society Myles Standish Hotel Boston

8 15 p m New England Pathological Society Boston Children's Hospital amphitheater (Vila Street)

FRIDAY OCTOBER 18

9-10 a m Recent Advances in Anesthesiology Dr F W Marvin Joseph H Pratt Diagnostic Hospital

SATURDAY OCTOBER 19

9-10 a m Hospital case presentation Dr S J Thannhauser Joseph H Pratt Diagnostic Hospital

*Open to the medical profession

OCTOBER 11 12 — Pan American Congress of Ophthalmology Page 898 issue of May 23

OCTOBER 14-25 — 1940 Graduate Fortnight of the New York Academy of Medicine Page 305 issue of August 22

OCTOBER 16 — Waltham Medical Meeting Page 557, issue of October 3

OCTOBER 20 — St Paul's Cathedral Notice above

OCTOBER 21 — American Board of Internal Medicine Page 369 issue of February 29

OCTOBER 25 — Staff meeting Massachusetts Memorial Hospitals Notice above

NOVEMBER 13 14 — New England Postgraduate Assembly Cambridge Massachusetts

NOVEMBER 14 — Pentucket Association of Physicians Page 263 issue of August 15

DECEMBER 2-29 — National Convention of the Association of Medical Students Boston

JANUARY 4 1941 — American Board of Obstetrics and Gynecology Page 1064 issue of June 20

MARCH 8 — American Board of Ophthalmology Page 201 issue of August 1

APRIL 21-25 — American College of Physicians Page 1065 issue of June 20

JUNE 2-6 — American Medical Association Cleveland Ohio

DISTRICT MEDICAL SOCIETIES

SUFFOLK

OCTOBER 30 — Page 604

NOVEMBER — Censors meeting Page 305 issue of August 22

JANUARY 29 — Page 604

APRIL 30 — Page 604

WORCESTER

NOVEMBER 13 — Grafton State Hospital, Grafton.

DECEMBER 11 — St. Vincent Hospital, Worcester.

JANUARY 8, 1941 — Worcester City Hospital, Worcester.

FEBRUARY 12 — Worcester State Hospital, Worcester.

MARCH 12 — Memorial Hospital, Worcester.

APRIL 9 — Hahnemann Hospital, Worcester.

Supper will be served at 6:30 p.m. followed by a business meeting and scientific program.

BOOK REVIEWS

The Electrocardiogram in Congenital Cardiac Disease. By Maurice A. Schnitker, B.Sc., M.D. 8° cloth, 147 pp., with 24 plates. Cambridge, Massachusetts: Harvard University Press, 1940. \$3.00.

The clinical recognition of certain patterns of congenital heart disease has come from a relatively recent correlation of the work of the practitioner and the pathologist. One aid to the clinician has been the electrocardiograph, but until the appearance of this book, the recorded experience in electrocardiography in proved cases of congenital heart disease has never been adequately reviewed and collected. The analysis of the data on which the book is based must have been a bewildering task because of the multiplicity of combined anomalies in so many of the cases and the difficulty in allocating the preponderant total cardiac effect to the principal lesion. A discussion of the physiology of the various anomalies provides an excellent basis for understanding the strains peculiar to specific regions in the heart and great vessels. One hundred and nine cases are reported, one hundred and six with autopsy, and one proved by surgical operation. The electrocardiograms are reproduced in one hundred and eight cases. The normal electrocardiogram in childhood is described first, and the congenital anomalies then considered in the acyanotic, late cyanotic and cyanotic groups. The author states: "With most lesions there is no specificity of electrocardiographic curves in a given group of similar cases. Group specificity was encountered only in congenital heart block, in dextrocardia with reversed chambers—either alone or as a part of generalized situs viscerum inversus—and in tricuspid valve disease, particularly tricuspid stenosis." However, correlations do occur often enough to be very significant in the diagnosis of other important groups.

The book will serve as a valuable reference work in determining the probable lesions in puzzling cases. The reviewer agrees with the author's statement, "The more refined and exact the diagnosis, the more accurately can we prognosticate, and the more intelligent will be our management of the patient with the malformed heart."

Diverticula and Diverticulitis of the Intestine. By Harold C. Edwards, M.S., London, F.R.C.S., Eng. 8°, cloth, 335 pp., with 223 illustrations, many in color. Baltimore: Williams & Wilkins Company, 1939. \$8.00.

The author of this interesting and excellent treatise on diverticulosis and diverticulitis of the intestine has presented in a clear-cut and forceful manner a subject which should be interesting to the surgeon and the internist alike. He considers such conditions in the duodenum and continues down the intestinal tract to the rectum. His opinions regarding the etiology and the pathology of diverticulosis and diverticulitis are well thought out. Indeed, this phase of the subject is presented in the most logical manner that the reviewer has yet seen. In particular, his explanation of the method of development from

the earliest stage of a diverticulum of the colon is well worth reading, and his drawings and photographs illustrate each phase distinctly.

The treatment of diverticulosis and diverticulitis occurring in different parts of the intestinal tract, as advocated by the author, is sound and conservative. A few minor exceptions might be taken to his medical management of diverticulosis of the colon, but these are of little significance.

Taken as a whole, the book is useful and readable; it deserves a place in modern medical literature.

Elmer and Rose Physical Diagnosis. Harry Walker, M.D. Eighth edition. 8°, cloth, 792 pp., with 295 illustrations. St. Louis: C. V. Mosby Company, 1940. \$8.75.

Any text which reaches its eighth edition must have merit. Dr. Walker's revision brings this old favorite fairly well up to date, and the book takes its place beside Cabot and Adams, Emerson, Sutton and the other comprehensive textbooks of physical diagnosis. The reviewer personally prefers to use a smaller, epitomized handbook for teaching purposes. A truly exhaustive monograph, such as that of Edens in German, is still lacking in English.

A few minor criticisms may be mentioned. Orthopercussion is incorrectly defined (page 222); "torsus" palatinus is correctly "torus" palatinus (page 72); it is questionable whether a detailed discussion of polygraphy any longer has a place in a textbook, since the procedure is certainly no longer in common use (pages 743-752); finally, the technic of joint examination is generally inadequate.

The book is printed on gray-blue tinted paper. This adversely affects its appearance, but may be restful to the student's eyes.

Doctors in Shirt Sleeves; Musings on Hobbies, Meals, Patients, Sport and Philosophy. Edited by Sir Henry Bashford. 8°, cloth, 294 pp. New York: Veritas Press, 1940. \$2.50.

For a number of years, the *Lancet* has published a column written by physicians, entitled "Grains and Scruples." The material now appears in book form, printed in Great Britain, but issued with a New York imprint. These papers were contributed by various members of the British medical profession on any subject that they desired. Most of them relate to physicians, their patients, their hobbies and their memories of the past. The articles tend to be philosophical essays, and as such are of considerable interest to the medical profession in general. Some are factual, such as the article by Squire Sprigge, on "Some Forgotten Medical Journal." Others treat on "The Biology of War," "Science and Spiritual Values," "Some Old Days in India," "On Hobbies" and "The Life of a Surgeon." There is something of interest in this volume for every reader. The papers naturally vary in both style and quality. The book would form a pleasing gift for a physician and would give him a few hours of pleasant relaxation.

Attaining Womanhood. By George W. Corner, M.D. 8°, paper, 92 pp. New York: Harper & Bros., 1939. \$1.00.

This little book is a companion volume to the author's similar book for boys, *Attaining Manhood*. A most satisfactory book in every way, it is well illustrated with simple, clear drawings emphasizing the various phases of reproduction. It undoubtedly is one of the best books for young girls to read and study.

The New England Journal of Medicine

Copyright 1940 by the Massachusetts Medical Society

VOLUME 223

OCTOBER 17, 1940

NUMBER 16

THE PREVENTION OF DIABETES*

REGINALD E. HAIST, M.D.,† JAMES CAMPBELL, Ph.D.,‡ AND CHARLES H. BEST, M.D.§

TORONTO, CANADA

WE have been emboldened by the results of our recent experiments, considered in relation to the work of Allen, Evans, Houssay, Young and others, to write an article under this provocative title. Although many years may be required to complete the obvious extensions of the present experiments, sufficient information is now available to show that the production of diabetes in experimental animals by the administration of pituitary diabetogenic substances may be prevented by dietary means or by the administration of large doses of insulin. Our studies have been concerned largely with the factors which affect the insulin content of the pancreas, and these findings support and extend those of previous workers, who have approached the same problem from other directions. The prevention of the diabetic condition by certain procedures makes it imperative that their curative effect also be thoroughly investigated.

PARTIAL PANCREATECTOMY

Minkowski, Hédon and others have shown that a very large portion of the pancreas must be removed before the diabetic condition appears. The beta cells of the islets of the pancreatic remnants in diabetic animals were shown by Homans¹ and Allen² to exhibit progressive degranulation and finally hydropic degeneration. Allen³ claimed that in the early stages of hydropic degeneration certain procedures permitted recovery of the islets, whereas after the condition had been present for a sufficient length of time the degenerated cells failed to recover and gradually disappeared. Fasting restored the damaged tissue to a normal con-

dition, if the diabetic state had not been present too long. Copp and Barclay⁴ found that the administration of insulin tended to promote recovery in islets showing the hydropic degenerative changes resulting from extensive partial pancreatectomy. They concluded also that there was a significant reduction in the insulin requirements

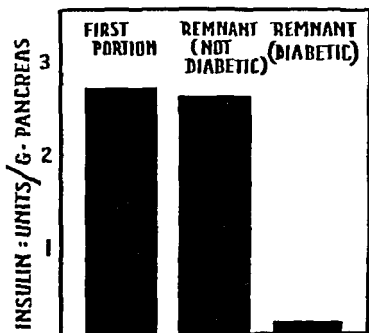


FIGURE 1 Insulin Content of the Pancreas in Dogs Following Partial Pancreatectomy

as the islet cells recovered granulation. These observations were confirmed and extended by Bowie.⁵ The results of the histological investigations, although not absolutely definite, strengthened the view that hydropic degeneration is the result of overstrain, and led to the conclusion that fasting or insulin administration tends to prevent it.

The conclusion that partial pancreatectomy increases the demands made on the remnant of pancreas is supported by the results of insulin assays (Haist and Best⁶). In partially pancreatectomized animals which had sufficient pancreas left to prevent the onset of diabetes, the insulin content per gram of the remnant of pancreas did not fall,

*From the Department of Physiology and the Department of Physiological Hygiene, University of Toronto.

Some of this material was presented by one of us (C. H. B.) as the Hugh H. Jackson Memorial Lecture at the Montreal Neurological Institute on April 3, 1940, and as a lecture before the Boylston Medical Society, Harvard Medical School, on May 13, 1940.

†Assistant professor of physiological hygiene, University of Toronto.

‡Research associate, Department of Physiology, University of Toronto.

§Professor of physiology, University of Toronto.

even though the amount of tissue remaining was very small. If, however, enough pancreas was removed to render the animal diabetic, the insulin concentration in the remnant was reduced to a very low value (Fig. 1).

Since diabetes was not evident in many dogs from which a large part of the pancreas had been removed, it would seem logical to assume that the total amount of insulin liberated had not been greatly decreased; and since the insulin content of

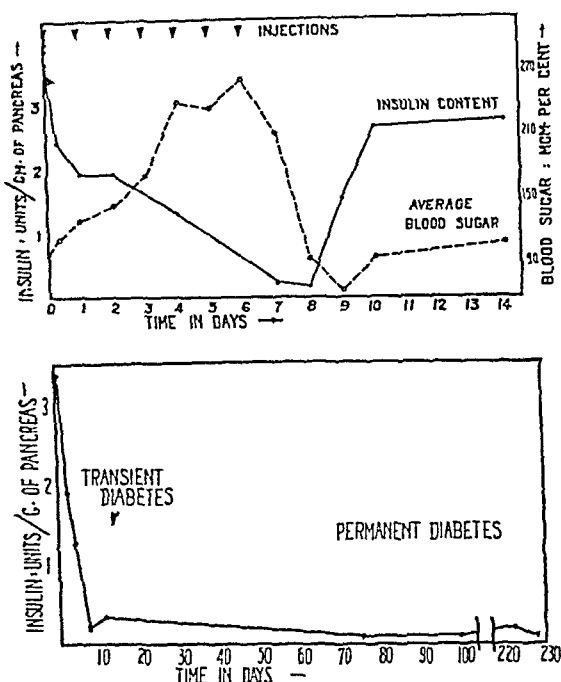


FIGURE 2. The Effect of Anterior-Pituitary Extract on the Insulin Content of the Pancreas and on the Blood-Sugar Level in Dogs.

the remnant did not fall, it would appear that the production of insulin was able to keep pace with its liberation. If these assumptions should prove to be correct, the production and liberation of insulin by the remnant over a given period must have increased. When the amount of tissue removed was still greater, the production of physiologically active insulin apparently was no longer able to keep pace with the liberation, and the insulin concentration in the remnant decreased. It therefore seems logical to consider that extensive partial pancreatectomy leads to hydropic degeneration of the islets and to reduction in the insulin content of the pancreas through overwork resulting from excessive demands on this organ for its internal secretion.

DIABETES INDUCED BY PITUITARY EXTRACTS

A condition of the pancreas similar to that found in the partially depancreatized animal is observed

in dogs receiving daily injections of anterior-pituitary extract (Richardson and Young⁷). Under these circumstances there is a gradual fall in the insulin content of the pancreas to very low levels (Best, Campbell and Haist⁸) (Fig. 2). At the same time there is a progressive degranulation of the beta cells of the islets, followed by hydropic degeneration (Richardson and Young⁷; Ham and Haist⁹). Here too the islet cells may recover on cessation of the injections and the insulin content may return to a normal value, if the degenerative condition has not been present for too long a period. The changes in insulin content and in the appearance of the islet cells are similar to those observed in partially depancreatized animals and are probably due to the same cause, namely, overwork. The chief difference is that in the condition produced by the anterior-pituitary extract the whole pancreas, rather than a remnant, is involved. In the condition resulting from partial pancreatectomy the reduction in the amount of functioning tissue seems to be the most important factor, whereas in the condition caused by the administration of the extract the increase in the need for endogenous insulin probably plays a major role. There is as yet no evidence to support the possibility that in

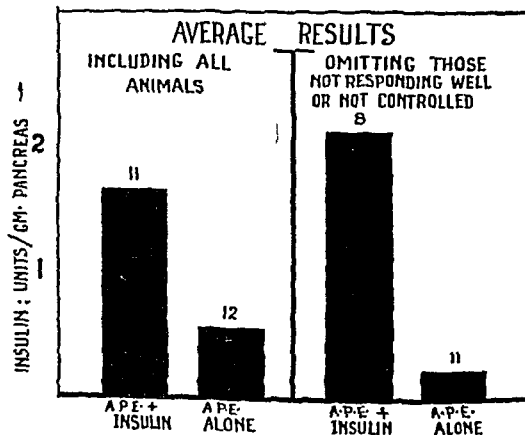


FIGURE 3. The Effect of Anterior-Pituitary Extract and Insulin and of Anterior-Pituitary Extract Alone on the Insulin Content of the Pancreas in Dogs.

the latter condition a reduction in the amount of functioning islet tissue results from a primary degenerative effect of the extract exerted directly on islet cells. There is evidence, however, that the need for insulin in these animals is increased. It has been shown (Houssay, Biasotti and Rietti¹⁰) that anterior-pituitary extract exerts its hyperglycemic and glycosuric effects in the absence of the pancreas, and that the injections of the extract antagonize the action of insulin even though the blood-sugar level is not elevated (Houssay and

Potick¹¹; di Benedetto¹²; Cope and Marks¹³). These observations indicate that the extract has profound extrapancreatic effects so long as administration is continued. Evidence of cellular proliferation and cytoplasmic changes in many organs other than the pancreas in animals injected with the extract is further proof of this influence (Ham and Haist¹⁴). It is reasonable to suppose that the need for endogenous insulin is increased by the extrapancreatic effects. This hypothesis is further substantiated by the finding that insulin administration tends to prevent the fall in insulin content and the degenerative changes resulting from the injections of anterior-pituitary extract (Campbell, Haist, Ham and Best¹⁴) (Fig. 3).

FACTORS INFLUENCING THE EFFECTS OF ANTERIOR-PITUITARY EXTRACT

In the previous section it was pointed out that insulin administration tends to prevent the degenerative effects and the lowering of the insulin content of the pancreas resulting from the administration of anterior-pituitary extract. Certain dietary factors also have a potent influence on the action of the extract. Houssay¹⁵ has reported that the hyperglycemic effect of the anterior-pituitary extract is not obtained in fasting dogs. We have recently confirmed this finding and have noted that the feeding of fat has a similar effect. Our experiments show too that fasting or fat-feeding tends to prevent the rapid fall in the insulin content of the pancreas and the degenerative changes in the islet cells resulting from the daily administration of anterior-pituitary extract. All the injected animals in our series were previously tested

ing from the daily injection of anterior-pituitary extract.*

The changes that occur during the administration of anterior-pituitary extract may be ascribed to the call on the pancreas for insulin, and may be prevented by lessening this demand. In the dog, the insulin content of the pancreas will return to normal and the islet cells will recover on cessation of the injections, provided the period of administration has not been too prolonged. If the injections are continued for sufficiently long periods and then stopped, the insulin content of the pancreas may remain permanently low and there is no recovery of islet cells. The beta cells degenerate and few if any are seen. Those that are present show a loss of granules. The permanent diabetic state probably results in large part from changes in the islet cells. In the transient type of diabetes observed while the extract is being administered, the islet-cell changes may be the result of the extrapancreatic effect, whereas in the condition of permanent diabetes which is present after the extract is discontinued, these changes, now permanent, are presumably responsible for the diabetes. The persistence of the condition therefore depends on the permanence of the change in the beta cells. If any procedure could cause recovery of the cells or lead to the formation of new ones, the condition would be cured. Fasting or fat-feeding (Young¹⁶; Marks and Young¹⁷; Dohan and Lukens¹⁸) relieves the diabetes in these animals, but as yet no conclusive proof has been given that such procedures restore the islet cells in the dog. Lukens and Dohan¹⁹ find that in the partially depancreatized cat made permanently diabetic by injections of anterior-pituitary extract, the administration of insulin leads to a recovery of the islet cells and cure of the diabetic state. As yet, no one has demonstrated that restoration of islet cells or the formation of new ones can occur in the permanently diabetic dog.

The islet and acinar cells of the pancreas are thought to have their origin in the cells of the duct epithelium. This is true in the embryo and under certain conditions in the adult organism. Allen³ found numerous vacuoles in the epithelium of the small ducts in partially depancreatized diabetic dogs. He suggested that the duct changes observed in these animals might represent an ex-

TABLE 1. *The Effect of Anterior-Pituitary Extract on the Average Insulin Content of the Pancreas in Dogs on Various Diets.*

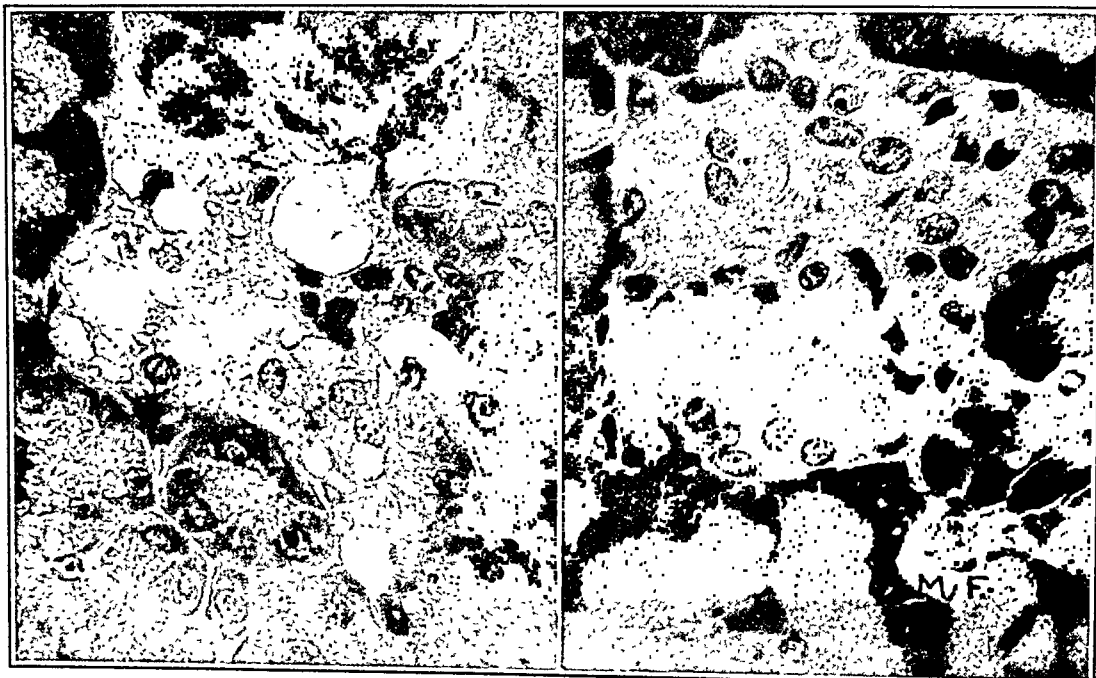
EXPERIMENTAL GROUP	INSULIN CONTENT OF PANCREAS units/gm
Normal diet plus anterior pituitary extract (7 days) — same caloric intake as fat group	0.5
Fat plus anterior pituitary extract (7 days)	1.7
Fasted plus anterior pituitary extract (7 days)	2.8
Fat fed (18 days)	2.5
Fasted (9 days)	2.6
Normal diet (9 days)	3.2

for their sensitivity to the extract. The various groups had the same average initial sensitivity. Average values for the insulin content of the pancreases of the three dogs in each group are shown in Table 1. It is evident from these figures that fasting or fat feeding tends to prevent the rapid fall in the insulin content of the pancreas result-

*The results on two other dogs are particularly interesting in this connection. One animal received a normal diet, the other had available only fat. While the second ingested moderately large amounts of fat during the first ten days, very small quantities were consumed during the latter part of the experiment. Both animals received daily injections of anterior pituitary extract for thirty days. The animal on the normal diet became permanently diabetic, the other showed no signs of diabetes when after the thirty days a normal diet was gradually restored. The animals are still under observation.

haustion of a proliferative rather than an endocrine activity. Similar vacuoles in the small ducts of the pancreas have been noted in animals showing the temporary diabetes and those showing the permanent diabetes resulting from the injection of anterior-pituitary extract (Richardson and Young⁷; Richardson²⁰; Ham and Haist⁹). This may be significant in connection with the failure of the islets to recover. The hope still remains, however, that proliferation without degeneration

though the degenerative effects were, in large part, prevented (Campbell, Haist, Ham and Best¹⁴) (Fig. 4). The hope is raised that proliferation without degeneration, produced by the administration of anterior-pituitary extract along with adequate amounts of insulin, may lead to an increase in the islet tissue and a more nearly normal islet function.* The same effect might be achieved by a pituitary principle causing only proliferation of the islet cells, the presence of which



A

B

FIGURE 4. *Histological Pancreatic Changes in Dogs.*

A shows hydropic changes in the islet, the dog having received anterior-pituitary extract alone.

B represents the islet in a dog that received anterior-pituitary extract and insulin. Note the mitotic figure in the acinus in the lower right-hand corner.

may lead to an increase in the islet tissue and a restoration of function in these animals. An increase in the islet tissue of normal animals as a result of the administration of anterior-pituitary extract has been noted by Anselmino, Herold and Hoffmann²¹ and, with a different extract, by Richardson and Young.²² In dogs treated with diabetogenic anterior-pituitary extract, proliferative changes were noted in the islets (Richardson and Young⁷) and also in the acini and ducts of the pancreas (Ham and Haist⁹). The finding of mitoses in ducts, acini and islets suggests that the mother cells of the ducts may be stimulated to differentiate into islet and acinar cells under the influence of the extract. It is important to note that the administration of insulin simultaneously with that of anterior-pituitary extract did not stop the proliferative changes, al-

though the degenerative effects were, in large part, prevented (Campbell, Haist, Ham and Best¹⁴) (Fig. 4). The hope is raised that proliferation without degeneration, produced by the administration of anterior-pituitary extract along with adequate amounts of insulin, may lead to an increase in the islet tissue and a more nearly normal islet function.* The same effect might be achieved by a pituitary principle causing only proliferation of the islet cells, the presence of which

is suggested by the recent work of Marks and Young.²³ We may summarize the points discussed thus far by stating that when a large portion of the pancreas is removed from dogs, the islets of the remnant become exhausted, probably through overfunction. In this case the overwork results from the fact that less pancreas is available. When the extract of anterior pituitary gland is given, the whole pancreas becomes exhausted, and the

*In this connection the results of a recent preliminary experiment by one of us (J. C.) are of interest. Two dogs which had exhibited intense diabetes for some fifty days after the cessation of injection of anterior-pituitary extract were given a second series of injections of the extract for ten days. While receiving this treatment the animals were fasted and then returned to exactly the same diet that they had previously received. The carbohydrate tolerance of one animal was only slightly changed, but a very dramatic improvement was found in the other. The permanence of this increased tolerance and the relative importance of the various factors involved in its production are as yet undetermined. It is obvious that the results of further experiments, in which histological and chemical studies on the pancreas before and after the "treatment" are included, will be most valuable.

overactivity probably results from the increased need for insulin, although a direct stimulation of the islets may play some part. When the islet changes become permanent and the injections are discontinued, the diabetes persists, because there is an inadequate number of functioning beta cells. The diabetic condition brought on by overstrain may be prevented or ameliorated by fasting, the feeding of fat or the administration of insulin. The fact that these procedures tend to reduce the activity of the islet cells is also indicated by some recent results that we have obtained.

EFFECT OF DIET ON THE INSULIN CONTENT OF THE PANCREAS

Fasting or feeding a diet of fat will lead to a definite reduction in the insulin content of the

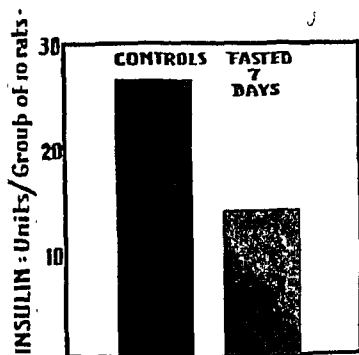


FIGURE 5. Total Insulin Units in the Pancreases of Normal and Fasted Rats.

pancreas of rats (Haist, Ridout and Best²⁴; Best, Haist and Ridout²⁵) (Figs. 5 and 6). Feeding a diet of sugar tends to prevent the fall in insulin content. When animals are paired and one group is fed with sugar and the other with fat to secure an equal caloric intake, at the end of fourteen days the insulin content of the pancreas in the sugar-fed group is much higher than that in the group receiving fat. The difference amounts to 42 per cent of the higher value. There is a moderate fall in the insulin content in the sugar-fed group. This is probably due to a reduced caloric intake, since male rats fed an inadequate amount of a balanced diet show a decrease in the insulin content of pancreas. The pancreases of the fasted or fat-fed rats do not show any marked degenerative change in sections stained with hematoxylin and eosin (Fig. 7), but granule studies have not yet been made.

In dogs, the effects of fasting or feeding of fat

on the insulin content of the pancreas are not so readily demonstrable as they are in rats. This is probably due to variations in age, previous history and so forth when dogs are used, and to the smaller number of animals employed. Also, the effective fasting period for the dog is much longer than that for the rat. The average insulin values for several fasting and fat-fed dogs treated for the times noted are given in Table 1. The individual values were all in the lower part of the normal range, but a much larger series than the present is necessary in order to demonstrate the effects of fasting or fat-feeding alone in this species.

When various diets are given to rats fasted for seven days it is found that a balanced diet results in the return of the insulin content of the pancreas to normal; a diet of sugar restores the content to within the normal range but the level is not maintained; fat, however, leads to no elevation in the insulin content above the fasting level but, if anything, occasions a further fall (Best, Haist and Ridout²⁵ (Fig. 8). It would appear that the insulin

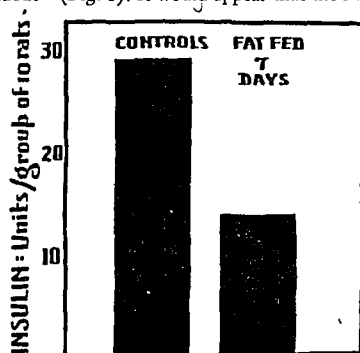


FIGURE 6. Total Insulin Units in the Pancreases of Normal and Fat-Fed Rats.

content of the pancreas is influenced in large part by the amount of available carbohydrate in the diet, although certain other factors are not as yet excluded.

HYPOPHYSECTOMY AND THE EFFECT OF DIET

The insulin content of the pancreas in rats hypophysectomized for twenty-six to sixty-six days is not greatly different from that of rats in control groups receiving the same caloric intake, although it is slightly less than that of controls fed *ad libitum* (Haist and Best⁶; Haist²⁶). The insulin content of the pancreas of hypophysectomized dogs is not abnormal, according to Chambers, Sweet and Chandler,²⁷ and we have confirmed this finding in four dogs.

The effect of fat-feeding on the insulin content of the pancreas can still be obtained in hypophysectomized rats (Haist and Best⁶; Haist²⁶). When a balanced diet is fed to hypophysectomized rats, previously fed fat for seven days, the insulin content is restored to normal (Fig. 9).

by the administration of insulin. The reduction in the rate of formation of physiologically active insulin is evidently greater than the decrease in the liberation of this material, and as a result the insulin content falls.

The daily administration of insulin to fasting

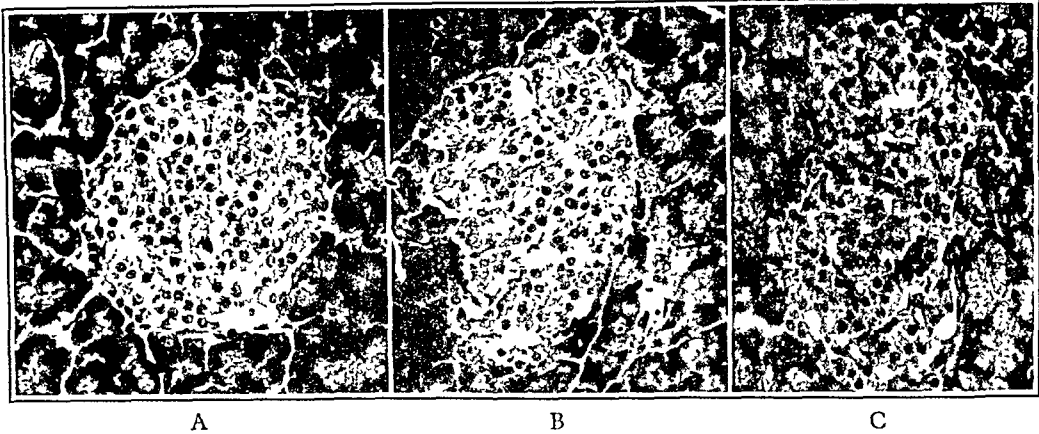


FIGURE 7. The Histological Differences in the Pancreatic Islets of Normal (A), Fasted (B) and Fat-Fed (C) Rats.

It would appear that the anterior pituitary gland is essential neither for the action of fat nor probably for that of starvation on the insulin content of the pancreas, although this does not preclude the possibility of some pituitary influence on the mechanism under normal conditions. Islet activity can

rats or to rats fed with fat leads to a much greater reduction in the insulin content of the pancreas than is occasioned by fasting or fat-feeding alone (Haist and Best^{6, 28}) (Figs. 11 and 12). It is clear that the administration of insulin does not prevent but increases the effect of fasting or fat-feeding on the insulin content of the pancreas. This should be compared with the effect of administering insulin in animals receiving injections of anterior-

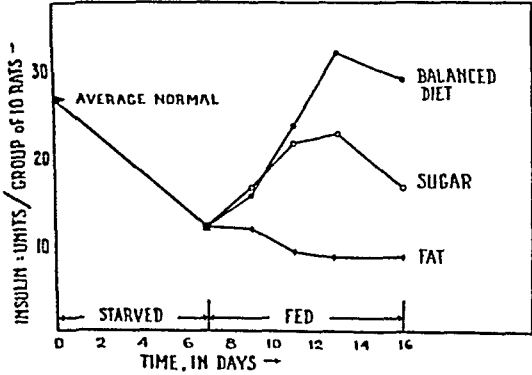


FIGURE 8. The Effect of Different Diets, Following Starvation, on the Insulin Content of the Pancreas in Rats.

therefore be depressed and restored in the absence of the pituitary gland.

EFFECT OF INSULIN

Administration of Insulin Greatly Affects the Insulin Content of the Pancreas

When large daily doses of protamine zinc insulin are given to rats fed the same amount of a balanced ration as are control animals, the insulin content of the pancreas is definitely lowered (Haist and Best²⁸) (Fig. 10). This observation suggests that the need for endogenous insulin is reduced

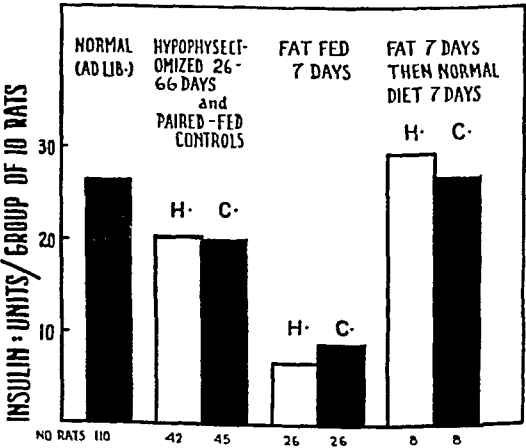


FIGURE 9. The Effect of Diet on the Insulin Content of the Pancreas in Hypophysectomized Rats.

pituitary extract. In this condition the administration of insulin prevents the fall in insulin content resulting from the injection of the extract (Fig. 13).

The effect of the insulin appears to be similar to that of fasting or fat-feeding and opposite to that of anterior-pituitary extract. The injection of

the latter or the removal of a very large portion of the pancreas makes the islets function more intensively, and may result finally in exhaustion and degeneration of the cells. Under these circumstances the insulin concentration in the pancreas probably falls because the production of insulin can no longer keep pace with its liberation. Fasting, fat-feeding and insulin have an opposite effect. They allow the pancreatic islets to rest and bring about a reduction in the insulin content of the pancreas. The insulin content under these conditions is probably reduced because the pro-

The alterations in insulin content with changes in diet occur under conditions that should also give rise to changes in tolerance. We have previously referred to the evidence for a reduced activity of the islets under these conditions. This change may affect sugar tolerance in different ways. One possibility is that when the islet activity is reduced, the immediate response of these cells to any sudden increase in the need for insulin is less than normal. An alternative explanation would be that when the level of insulin liberation is low, that is, when the continuous outpouring of the hormone is reduced, the tissues and especially the liver are altered so far as their response to sugar is concerned. Hence it can be seen that regardless of whether the pancreas or the liver is considered to play the major role in determining sugar tolerance, the level of activity of the islet cells may be of great importance. It seems logical to assume that the reduced activity of the islets under the conditions mentioned is in some way responsible for the lowered tolerance to sugar noted under similar conditions. This is substantiated by the fact that insulin administration, which, as previously pointed out, leads to reduced islet activity, also produces a decreased sugar tolerance

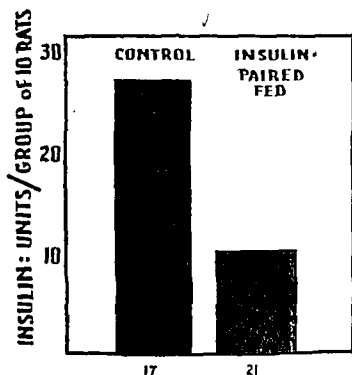


FIGURE 10. The Effect of Insulin on the Insulin Content of the Pancreas in Normally Fed Rats.

The numbers under the blocks represent the total number of animals.

duction of the hormone is decreased to a greater extent than is its liberation.

Relation to Other Observations on the Effect of Diet and Administration of Insulin

The experiments on rats which we have just cited indicate that fasting, fat-feeding and the administration of insulin not only allow the islets to rest, but also afford an explanation of certain other phenomena that occur when such procedures are employed. It has been known for a long time that changes in the response to administered carbohydrate are apparent in animals fasted or fed with fat for a sufficient period. (For a review of this subject, see Chambers.²⁹) Such animals show a reduced tolerance for sugar, as evidenced by the higher, more prolonged blood-sugar curve, glycosuria and the absence of the normal rise in the respiratory quotient following the administration of glucose. The administration of carbohydrate restores the tolerance to normal. Some of these changes have been observed in the hypophysectomized dog.²⁹

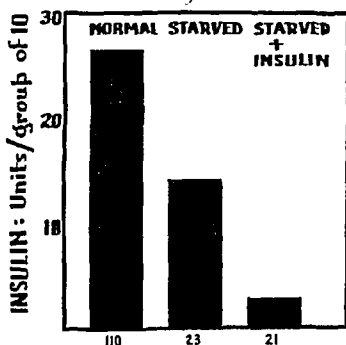


FIGURE 11. The Effect of Insulin on the Insulin Content of the Pancreas in Fasted Rats.

(Wilder, Smith and Sandiford³⁰; Clark, Gibson and Paul³¹; Maher and Somogyi³²; Looney and Cameron³³).

APPLIED PHYSIOLOGY

In considering the relation of our results to the treatment of diabetes in human subjects, we may assume that the factors which prevent the condition from developing will also tend to limit its progress. As we have pointed out, the procedures which permit the pancreatic islets to rest, namely,

fasting, fat-feeding, and the administration of insulin, prevent or hinder the development of the diabetic state under experimental conditions. These procedures affect the pancreas in a manner opposite to that of high-carbohydrate diets, and prevent the deleterious effects of anterior-pituitary diabetogenic principles. There is no evidence as yet that the factors which rest the pancreas cause permanent damage to islet cells, whereas there is adequate proof that factors leading to overactivity may produce permanent changes. If a clinician is convinced that the patient will be benefited

idle beta cell is not much better than an absent one. Temporarily, this may be true. But rest restores the cells and makes possible a better islet function in the future. The resting procedures, then, serve two purposes: they prevent the degenerative changes from occurring in cells not already affected; and they permit the restoration of those exhausted cells which still retain their ability to recover.

If it is thought that protection is needed, the best clinical procedure must be chosen. Wide departures from the normal diet are permissible for only short intervals. Over longer periods nutritional requirements must, of course, be satisfied. This is particularly true for growing children, who must have a palatable diet providing an adequate caloric intake and all the essential food factors. Under these circumstances only minor alterations in diet may be justifiable and the administration of insulin may be the method of choice.

There is considerable evidence that heredity plays an important role in the incidence of diabetes (Pincus and White³⁴). A procedure which would allow early diagnosis and treatment in children with a family history of diabetes would be the determination of blood sugars at very frequent intervals. Prevention, however, would be better than

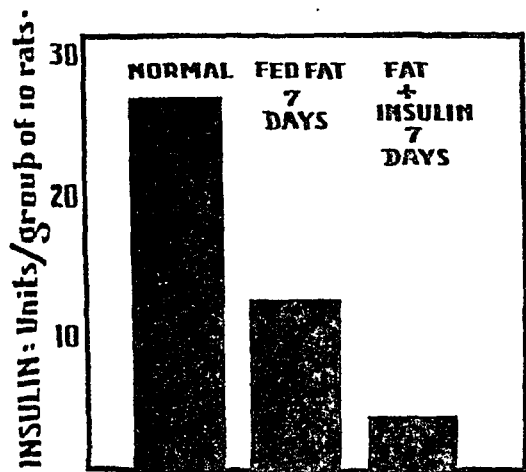


FIGURE 12. *The Effect of Insulin on the Insulin Content of the Pancreas in Fat-Fed Rats.*

by stimulation of the islet cells, diets rich in carbohydrate are obviously indicated. It will be remembered that when such diets are used in experimental animals, the islet cells may be protected by the provision of large amounts of insulin. If, on the other hand, the clinician believes that a useful purpose will be served by resting the pancreas, fasting, fat-feeding and the administration of insulin may be employed. When there is already very extensive islet-cell destruction, he may decide that there is no point in resorting to these procedures. Under other conditions, however, a reduction of the strain on the remaining islets may allow the restoration of some exhausted cells and thus improve the diabetic condition. This would seem to be particularly true in the early stages of the disease. In experimental animals the exhausted cells retain for an appreciable length of time their ability to recover. Lukens and Dohan¹⁰ have obtained evidence that this period is much longer in the cat than it is in the dog. In man, the interval during which the cells may be exhausted but still remain capable of recovery is unknown. It might be argued that a resting or

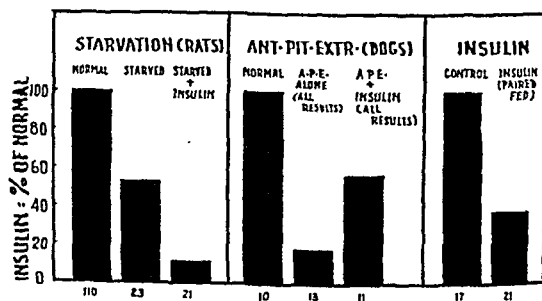


FIGURE 13. *The Effect of Insulin on the Insulin Content of the Pancreas in Different Animals under Varying Conditions.*

cure. The prophylactic administration of insulin to potential diabetic patients may become an accepted clinical procedure in the future. We suggest that the incidence of diabetes should be investigated in two large and comparable groups of children with a family history of this disease. One group should be given a normal diet and the second a diet as low in carbohydrate and protein and as rich in fat as is feasible with the above-mentioned limitations in view. This second group might receive insulin in the limited amounts which may safely be given under these conditions. We appreciate the difficulties inherent in this type of

clinical investigation, but believe that the goal justifies the endeavor.

SUMMARY

Extensive partial pancreatectomy or the daily administration of anterior pituitary extracts, in dogs, causes a great reduction in the insulin content of the pancreas, which is associated with hydropic degenerative changes in the islets.

Fasting, fat feeding or insulin administration, in rats, leads to a decrease in the insulin content of the pancreas, but this is not associated with degeneration in the islet cells.

The daily administration of protamine zinc insulin augments the effect of fasting or fat feeding, giving a still further reduction in the insulin content. It has also been shown that daily injections of protamine zinc insulin in animals receiving anterior pituitary extract tend to prevent the reduction in the insulin content and the degenerative islet changes produced by the extract alone. The feeding of fat, or fasting, also prevents these effects of the extract.

From these and other considerations mentioned in the paper we conclude that extensive partial pancreatectomy and the administration of anterior pituitary extract lead to the exhaustion of the islets, largely through overwork, whereas fasting, fat feeding and insulin administration allow the islets to rest. These latter procedures inhibit the diabetogenic action of the anterior-pituitary extract and thus prevent the onset of diabetes. The clinical applications of these findings are discussed.

It will be clear to all who read this article that the results of recent studies emphasize the great importance of the work which Dr. Frederick M. Allen previously carried out in this same general field. It is a pleasure also to acknowledge the stimulating and helpful influence which Dr. Elliott P. Joslin has exerted on many of us who have attempted to increase the knowledge and understanding of the diabetic state.

REFERENCES

- Homans J. The relation of the islets of Langerhans to the pancreatic acini under various conditions of secretory activity. *Proc Roy Soc London Ser B* 86:73-87, 1913.
- Allen F. M. *Studies Concerning Glycosuria and Diabetes*. 1179 pp. Cambridge, Massachusetts: Harvard University Press, 1913.
- Idem. Pathology of diabetes. I. Hydropic degeneration of islets of Langerhans after partial pancreatectomy. *J Metabolic Research* 1:541, 1922. Pathology of diabetes. IV. Role of hyperglycemia in production of hydropic degeneration of islets of Langerhans. *Ibid* 1:588, 1922.
- Copp E. F. P. and Barclay A. J. The restoration of hydropically degenerated cells of the pancreas in dogs under insulin treatment. *J Metabolic Research* 4:445-451, 1923.
- Bowie D. J. unpublished data.
- Haist R. E. and Best C. H. Factors affecting the insulin content of pancreas. *Science* 91:410, 1940.
- Richardson K. C. and Young F. G. Histology of diabetes induced in dogs by injection of anterior pituitary extracts. *Lancet* 1:1098-1101, 1938.
- Best C. H., Campbell J. and Haist R. E. The effect of anterior pituitary extracts on the insulin content of the pancreas. *J Physiol* 97:200-206, 1939.
- Ham A. W. and Haist R. E. Histological effects of diabetogenic anterior pituitary extracts. *Nature* 144:835, 1939.
- Houssay B. A., Bassotti A. and Retic C. T. Action diabetogène de l'extrait antéhypophysaire. *Compt rend Soc de biol* 111:479, 1932.
- Houssay B. A. and Potock D. Antagonisme entre l'hypophyse et l'insuline chez le crapaud. *Compt rend Soc de biol* 101:940-942, 1929.
- Benedetto E. Extrait antéhypophysaire et résistance à l'insuline. *Compt rend Soc de biol* 112:499-501, 1933.
- Cope O. and Marks H. P. Further experiments on the relation of the pituitary gland to the action of insulin and adrenaline. *J Physiol* 83:157-176, 1935.
- Campbell J., Haist R. E., Ham A. W. and Best C. H. The insulin content of the pancreas as influenced by anterior pituitary extract and insulin. *Am J Physiol* 129:328, 1940.
- Houssay B. A. and Haist R. E. Diabetes as a disturbance of endocrine regulation. *Am J Med Sci* 193:581-606, 1937.
- Young F. G. The anterior pituitary gland and diabetes mellitus. *New Eng J Med* 221:635-646, 1939.
- Marks H. P. and Young F. G. Observations on the metabolism of dogs made permanently diabetic by treatment with anterior pituitary extract. *J Endocrinology* 1:470-510, 1939.
- Dobson F. C. and Lukens F. D. W. Further observations on the permanent diabetes produced by anterior pituitary extract. *Am J Physiol* 126:478, 1939.
- Lukens F. D. W. and Dobson F. C. Morphological and functional recovery of the pancreas in dogs in diabetes treated with insulin. *Science* 92:222, 1940.
- Richardson K. C. The influence of diabetogenic anterior pituitary extracts on the islets of Langerhans in dogs. *Proc Roy Soc London Series B* 128:153-169, 1940.
- Anselm no. K. J. Herold L. and Hoffmann F. Ueber die pankreatropische Wirkung von Hypophysenvorderlappeneextrakten. *Ann Nch schr* 12:1245-1247, 1933.
- Richardson K. C. and Young F. G. The pancreatotropic action of anterior pituitary extracts. *J Physiol* 91:352-364, 1937.
- Marks H. P. and Young F. G. The hypophysis and pancreatic insulin. *Lancet* 1:493-497, 1940.
- Haist R. E., Ridout J. and Best C. H. Diet and the insulin content of the pancreas. *Am J Physiol* 126:518, 1939.
- Best C. H., Haist R. E. and Ridout J. Diet and the insulin content of pancreas. *J Physiol* 97:107-119, 1939.
- Haist R. E. The pituitary and the insulin content of pancreas. *J Physiol* 98:419-423, 1940.
- Chambers W. H., Sweet J. E. and Chandler J. P. Carbohydrate metabolism in the hypophysectomized dog. *Am J Physiol* 113:76, 1935.
- Haist R. E. and Best C. H. unpublished data.
- Chambers W. H. Undernutrition and carbohydrate metabolism. *Physiol Rev* 18:248-296, 1938.
- Wilber R. M., Smith F. H. and Sandford I. Observations on obesity. *Ann Int Med* 6:174-182, 1932.
- Clark B. B., Gibson R. B. and Paul W. D. A study of the role of insulin in metabolism in nondiabetic patients. *J Lab & Clin Med* 1:1-14, 1933.
- Looney J. M. and Cameron D. E. Effect of prolonged insulin therapy on glucose tolerance in achroplastic patients. *Proc Soc Exper Biol & Med* 37:253-257, 1937.
- Penick G. and White P. On the inheritance of diabetes mellitus in a family of 12 hundred and seventy five family histories. *Am J Med Sci* 186:1-14, 1933.

THYROGLOSSAL CYSTS AND SINUSES*

A Study and Report of 198 Cases

ROBERT E. GROSS, M.D.,† AND MARION L. CONNERLEY, M.D.‡

BOSTON

MIDLINE cervical cysts and sinuses arising from the thyroglossal duct are often encountered in childhood. These lesions are of importance because of disfigurements which they produce

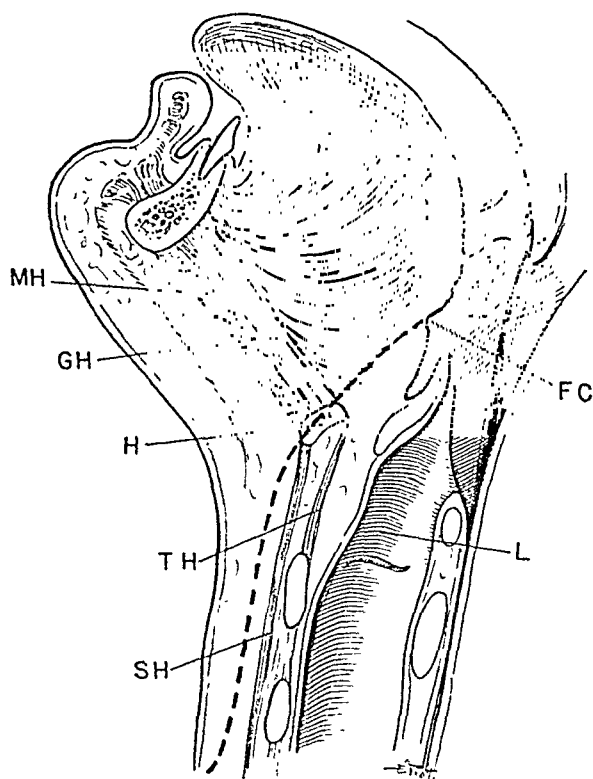


FIGURE 1.

Sagittal section through the tongue, larynx and neck, showing the position of structures related to thyroglossal cysts and sinuses which may occur anywhere along the dotted line. FC = foramen cecum; GH = geniohyoid muscle; H = hyoid bone; L = larynx; MH = mylohyoid muscle; SH = sternohyoid muscle; TH = thyrohyoid membrane.

and because they may be the seat of recurring inflammatory disease. It is the purpose of this paper to review and report the findings from 198 cases observed or treated at the Children's Hospital.

EMBRYOLOGICAL CONSIDERATIONS

In embryos of 1.5 or 2.5 mm., the thyroid anlage appears as a midline structure projecting down-

*From the Surgical Clinic, Children's Hospital, and the Department of Surgery, Harvard Medical School.

†This publication was aided by a grant from the Godfrey M. Hyams Trust.

‡Associate in surgery, Harvard Medical School; associate visiting surgeon, Children's Hospital.

*Surgical house officer, Children's Hospital.

ward between the first and second branchial arches. The stalk of this anlage has an attachment at the tuberculum impar, which later becomes the foramen cecum. The thyroid anlage descends in the neck but maintains its superior connection by the long thyroglossal duct. Toward the latter half of the second month, the developing hyoid bone divides the thyroglossal duct into upper and lower portions which subsequently atrophy and disappear by the end of the eighth week. Rests of cells may remain anywhere along this tract and give rise to postnatal development of cysts (Fig. 1). By pressure necrosis of overlying skin or by supuration during a superimposed inflammation, such a cyst may attain an external cutaneous opening and thereby be transformed into a fistula.

PATHOLOGY

Thyroglossal cysts or sinuses are lined by an epithelium which is usually columnar or ciliated, but which may be squamous in type. Like the cysts, the sinuses may have a flat and rather level epithelial lining, but not uncommonly there are small slit-like or irregularly branched side pockets extending for several millimeters into the surrounding tissues. The cyst or sinus usually contains some mucoid material which has been secreted by its lining cells; but if squamous cells form a part of the epithelial lining, yellow grumous or pasty material may be found in the lumen. Varying degrees of acute and chronic inflammation are found in the walls, particularly those of the sinuses.

Microscopic sections of the central part of the hyoid bone from these cases often show an irregular or branching epithelium-lined tract directly piercing the bone or its periosteum. It may be impossible to detect this abnormality by gross inspection, palpation or probing. Likewise, study of soft tissues removed *en bloc* above or below the hyoid bone, and yet above the gross cyst or sinus, often shows microscopic-sized tracts which were unsuspected by the surgeon. The thorough operator, therefore, must always remove a block of tissue upward as far as the foramen cecum and must remove the central part of the hyoid bone, even though he cannot see or feel any tract in these structures.

CLINICAL FINDINGS

In approximately 85 per cent of our patients the lesions were cysts, and in about 15 per cent they were sinuses. In a few cases there was a cyst in the deeper portions of the neck and a superficial sinus which opened on the skin. Such a sinus may or may not connect with the cystic structure.

tract leading to the base of the tongue. If the cyst is freely movable it may not ride directly in the midline but slide off slightly to one side of the trachea or the larynx (Fig. 7). Because of the overlying cervical fascia, the cysts usually do not transilluminate well, in spite of the fact that they may contain clear fluid.

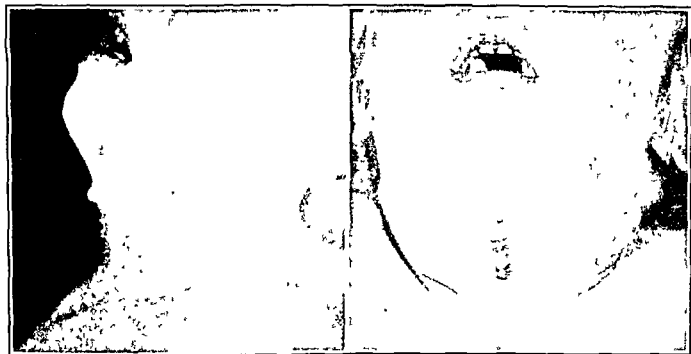


FIGURE 2.

A five-year old girl with a vertical, midline, reddened area of mucous membrane which had been present since birth. This represents a thyroglossal sinus which has extensively opened along its anterior edge, thus presenting the mucous membrane to view.

In some cases a midline cyst had been present for a considerable period of time before it subsequently attained a cutaneous opening. In 2 cases there were vertical midline linear cutaneous lesions, in each of which a long sinus appeared to have opened anteriorly so as to expose a long piece of raw mucous membrane (Figs. 2 and 3).

A thyroglossal cyst may be found anywhere in the midline cervical structures from the base of the tongue downward to the suprasternal notch (Figs. 4 and 5). The cyst may be as small as a pea, or as large as a flattened golf ball. An average cyst is 1 to 2 cm. in diameter (Fig. 6). In general, the cysts are smoothly rounded and have a well-defined border, but the larger ones are apt to be compressed by overlying skin or fascia. The larger cysts can be moved only slightly, but the smaller ones can be readily displaced upward and downward and also from side to side. As a rule they are nontender, unless there has been some superimposed infection. Almost invariably there is some deep attachment to structures in the base of the mouth or to the underlying hyoid bone, whereas they are unattached to the overlying skin. In rare cases pressure on the cyst will express a small amount of fluid into the throat by way of a

In 3 cases there was a small swelling at the base of the tongue, for treatment of which the patients entered the Nose and Throat Department. These proved to be thyroglossal cysts 0.8 to 1.5 cm. in diameter which lay just beneath the foramen cecum.

Thyroglossal-duct sinuses open in the midline, anywhere from the suprasternal notch upward to a position just in front of the hyoid bone. In most cases careful palpation of the neck will reveal a cord of tissue running upward in the deep structures of the neck, and an attachment to the hyoid bone can often be made out. The cutaneous openings are from 1 to 3 mm. in diameter (Fig. 8). The skin around the opening usually shows some degree of chronic inflammation. From time to time, droplets of fluid, which are either clear, glairy and mucoid or cloudy, thin and yellowish, may exude from the sinus. The latter type of fluid may be purulent exudate or may be desquamated cells from a squamous epithelial lining. Therefore, a yellowish discharge does not necessarily mean that infection is present.

Figure 9 shows the year in which a cyst or sinus was first noted in our 110 patients who were subsequently operated on. In 29 per cent of the cases the lesions were noted at birth, and in 76 per cent

THYROGLOSSAL CYSTS AND SINUSES*

A Study and Report of 198 Cases

ROBERT E. GROSS, M.D.,† AND MARION L. CONNERLEY, M.D.‡

BOSTON

MIDLINE cervical cysts and sinuses arising from the thyroglossal duct are often encountered in childhood. These lesions are of importance because of disfigurements which they produce

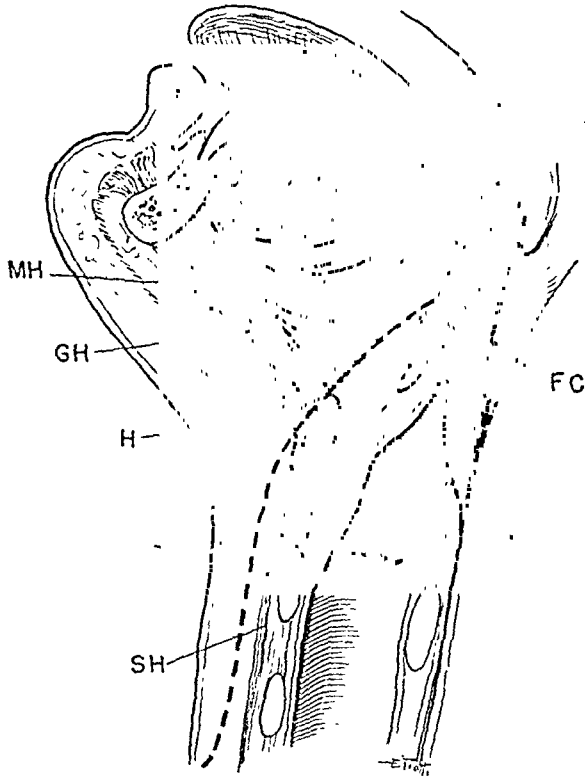


FIGURE 1.

Sagittal section through the tongue, larynx and neck, showing the position of structures related to thyroglossal cysts and sinuses which may occur anywhere along the dotted line. FC = foramen cecum; GH = geniohyoid muscle; H = hyoid bone; L = larynx; MH = mylohyoid muscle; SH = sternohyoid muscle; TH = thyrohyoid membrane.

and because they may be the seat of recurring inflammatory disease. It is the purpose of this paper to review and report the findings from 198 cases observed or treated at the Children's Hospital.

EMBRYOLOGICAL CONSIDERATIONS

In embryos of 1.5 or 2.5 mm., the thyroid anlage appears as a midline structure projecting down-

ward between the first and second branchial arches. The stalk of this anlage has an attachment at the tuberculum impar, which later becomes the foramen cecum. The thyroid anlage descends in the neck but maintains its superior connection by the long thyroglossal duct. Toward the latter half of the second month, the developing hyoid bone divides the thyroglossal duct into upper and lower portions which subsequently atrophy and disappear by the end of the eighth week. Rests of cells may remain anywhere along this tract and give rise to postnatal development of cysts (Fig. 1). By pressure necrosis of overlying skin or by supuration during a superimposed inflammation, such a cyst may attain an external cutaneous opening and thereby be transformed into a fistula.

PATHOLOGY

Thyroglossal cysts or sinuses are lined by an epithelium which is usually columnar or ciliated, but which may be squamous in type. Like the cysts, the sinuses may have a flat and rather level epithelial lining, but not uncommonly there are small slit-like or irregularly branched side pockets extending for several millimeters into the surrounding tissues. The cyst or sinus usually contains some mucoid material which has been secreted by its lining cells; but if squamous cells form a part of the epithelial lining, yellow grumous or pasty material may be found in the lumen. Varying degrees of acute and chronic inflammation are found in the walls, particularly those of the sinuses.

Microscopic sections of the central part of the hyoid bone from these cases often show an irregular or branching epithelium-lined tract directly piercing the bone or its periosteum. It may be impossible to detect this abnormality by gross inspection, palpation or probing. Likewise, study of soft tissues removed *en bloc* above or below the hyoid bone, and yet above the gross cyst or sinus, often shows microscopic-sized tracts which were unsuspected by the surgeon. The thorough operator, therefore, must always remove a block of tissue upward as far as the foramen cecum and must remove the central part of the hyoid bone, even though he cannot see or feel any tract in these structures.

*From the Surgical Clinic, Children's Hospital, and the Department of Surgery, Harvard Medical School.

†This publication was aided by a grant from the Godfrey M. Hyams Trust. ‡Associate in surgery, Harvard Medical School; associate visiting surgeon, Children's Hospital.

§Surgical house officer, Children's Hospital

Dermoid or sebaceous cysts in the midline of the neck are attached to the overlying skin, in contrast to the thyroglossal cyst, which has a deep anchorage.

TREATMENT

Before considering treatment in these cases, it is well to state that we do not believe that all thyroglossal cysts should be removed. During the period in which our 110 cases have been surgically treated, 88 additional patients who presumably had small thyroglossal cysts have been examined and observed, and have not been operated

Since all the treated cases in this series were children, general anesthesia, either by ether or by Avertin and ether, was employed. However, in older age groups local or block anesthesia would undoubtedly be satisfactory. With the patient lying on the table, the trunk should be slightly raised and the head well extended. Midline vertical incisions are contraindicated because the subsequent scar is unsightly and a midline contracture which is extremely difficult or impossible to eradicate may result. A transverse incision should always be made and great care employed in the selection of the site of the incision, in order to



FIGURE 5

A four-year-old girl with a small, low, thyroglossal cyst which had been present for one year.

on. In these cases operation was advised against because the cysts did not enlarge appreciably or because disfigurement was minimal. It is possible that some of these patients may come to subsequent surgery. While we have thus deferred operation for these small cysts, we have always advised operative excision of the sinuses because of the high probability of recurring infection.

We do not believe in the treatment of thyroglossal sinuses or cysts by the use of sclerosing or cauterizing agents, because it is unreasonable to expect that injected fluids will reach all the epithelial-lined side pockets that can be found on histological examination of many of these specimens.

In 11 of our patients an infected and suppurating cyst had to be incised and drained before radical removal could be undertaken.

make sure that it exactly falls in the folds of the neck and extends equidistantly to each side of the midline. The incision can rarely be shorter than 2 cm. if good exposure is to be obtained in the deeper portions of the neck, and it may have to be twice this length if the child is large or the cyst is big. If a cutaneous sinus is present, a transverse elliptical incision is made so as to include the cutaneous orifice. Freeing the cyst or sinus usually offers no difficulty unless there has been severe inflammation in the regional tissues.

For the inexperienced operator there is often a temptation to remove only the presenting cyst or the presenting sinus as far as the hyoid bone. There are doubtless some cases in which this incomplete procedure will result in permanent cure. However, we and others have learned that to do this leads frequently to recurrences

which are more difficult to handle at secondary operations. Therefore, it cannot be emphasized too strongly that the only proper treat-

Figure 10 indicates the successive operative steps. In 1 there is a transverse incision over a presenting midline cyst. In 2 this has been carried down



FIGURE 6.
Photographs of surgically removed thyroglossal cysts.

ment must always include removal of about 1 cm. of the hyoid bone and in addition a block of tissue up to the base of the tongue. This more ex-

through subcutaneous fat and platysma muscle. In 3 the cyst is grasped with a clamp and exteriorized to show better the deep cervical fascia which

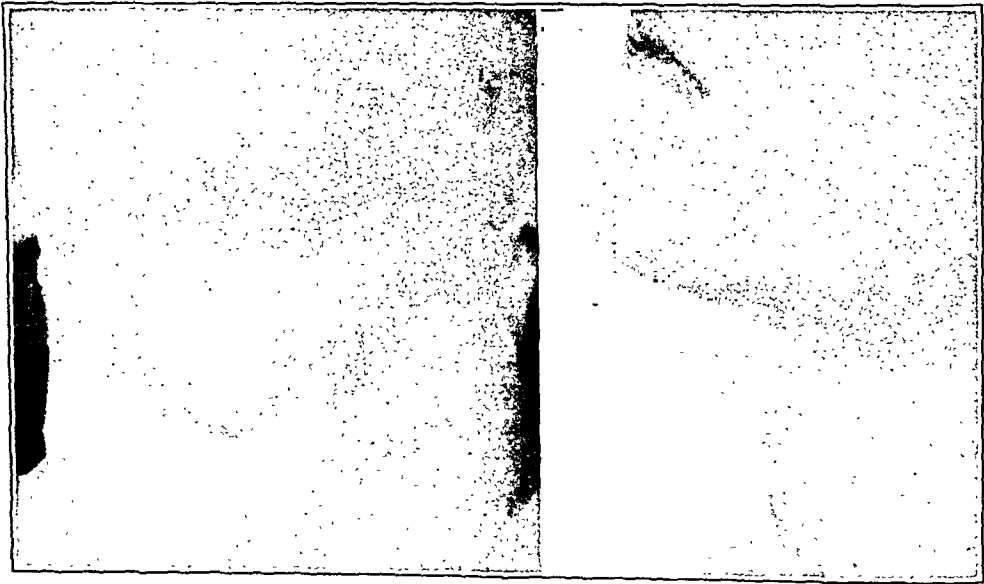


FIGURE 7.
A five-year-old girl with a thyroglossal cyst which had been present for three years. In the anterior view the cyst is seen to be displaced slightly from the midline.

tensive operation does not appreciably increase the length of the operation, and if it is routinely carried out, recurrences will be rare; indeed they were absent in our series.

extends up over the cyst. This fascia is cut around the base of the cyst, so that a stalk is brought into view as shown in 4. In 5 the presenting muscles are cleared from the overlying structures

and the fibers of the mylohyoid muscles of either side can be seen coursing obliquely to meet in the midline. Below the stalk, the longitudinal fibers

wound, and attached to it is a stalk of tissue, as shown. A forefinger of the anesthetist or an assistant, passed into the mouth and pressing in the



FIGURE 8.

A ten-year-old girl with a thyroglossal-duct sinus. The discharging fistula had been noted for three years.

of the ribbon muscles (sternohyoid) are brought into view. At the junction of these two groups of muscles the hyoid bone is now seen or palpated. In young subjects the external surface of the bone can be viewed, but in more muscular or older individuals the hyoid bone may be more deeply imbedded. In 6 the hyoid bone is grasped with an Allis clamp just to one side of the midline and the bone is pulled forward. It is then cut with a scalpel in the patients less than two or three years of age, but it must be severed with bone cutters in older subjects. In 7 the hyoid bone has been cut on both sides and traction on the cyst will pull forward the centrally freed portion of hyoid bone. One blade of the scissors can then be pushed inward as far as the thyrohyoid membrane and a circular cut of all the muscles can be rapidly made, so that a fringe of musculature is left on the centrally placed block of tissue. If one does not know the regional anatomy well, there may be some hesitation at this step, for fear of entering the mouth. However, the thyrohyoid membrane is a distinct grayish-yellow structure which can be readily identified and dissected from the overlying musculature. Rather than make many cuts through the muscles to get down to this membrane, it is best to puncture through the muscles at one point as far as the membrane, and then to sweep the scissors around, severing a full thickness of musculature in each cut. In 8 the thyrohyoid membrane forms the floor of the

region of the foramen cecum, will show that the base of the stalk is separated from the finger in

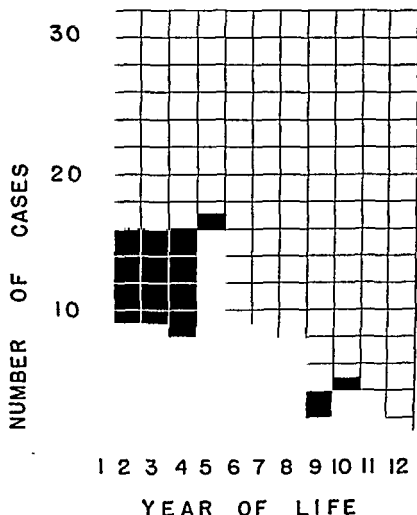


FIGURE 9.

A graph showing the ages at which symptoms were first noticed in 110 surgically treated cases of thyroglossal cyst or sinus. Seventy-six per cent of the patients had symptoms before they were six years of age.

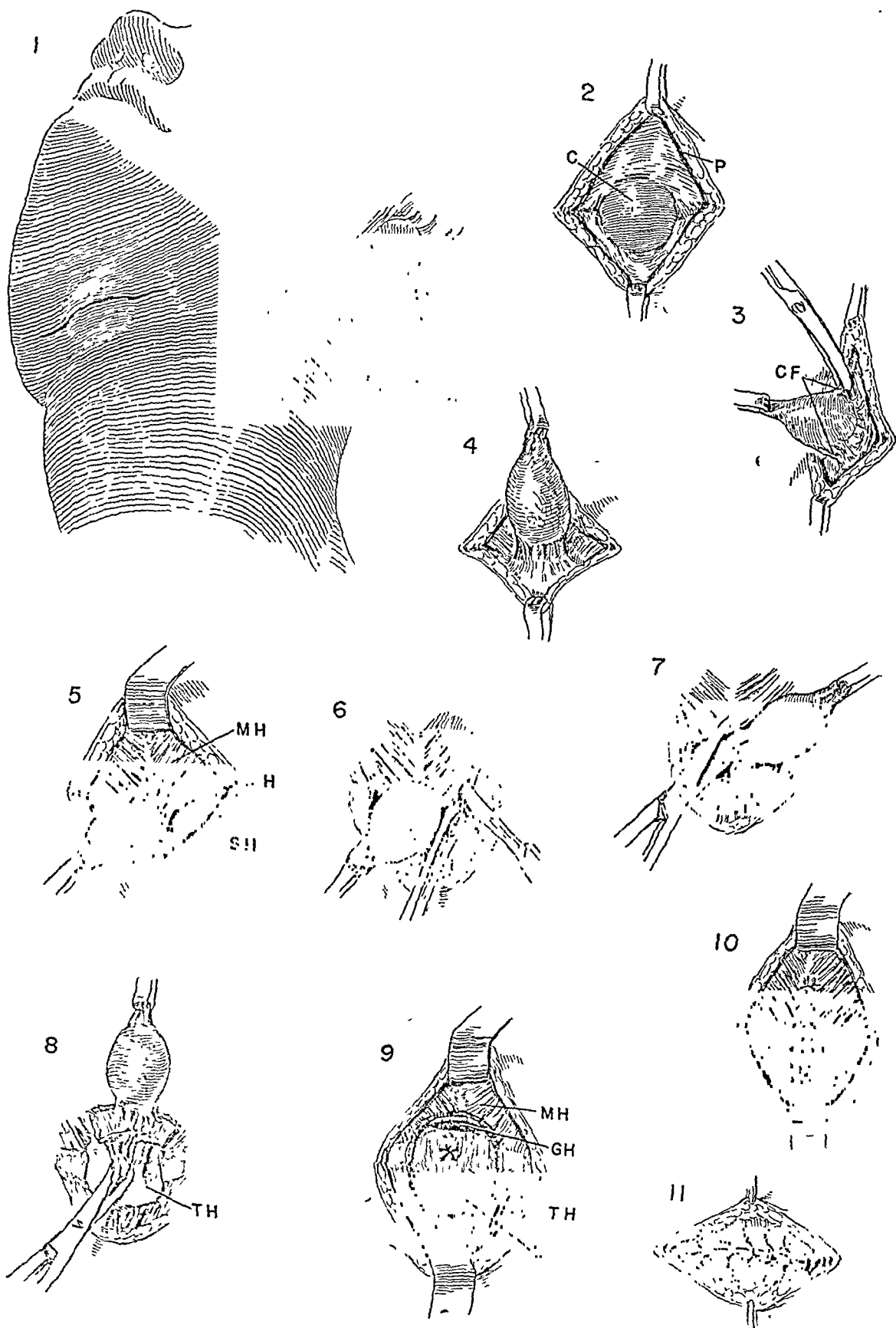


FIGURE 10.

Sketch of the steps in the operative removal of a thyroglossal cyst (or sinus), which are described in the text. C = cyst; CF = cervical fascia; GH = geniohyoid muscle; H = hyoid bone; L = larynx; MH = mylohyoid muscle; P = platysma muscle; SH = sternohyoid muscle; TH = thyrohyoid membrane.

the mouth by only a few millimeters of tissue. When the dissection has been carried to this complete extent the stalk may be cut across. In 9 a figure-of-eight suture or a purse-string suture is placed so as to invert the local tissue into the mouth. In 10 the musculature is brought together in the midline with interrupted sutures of fine silk or fine chromic catgut. No attempt need be made to approximate the ends of the bone, and indeed, even if they do not butt against one another no subsequent derangement in the action of the local muscles will be noticed. In 11 the platysma muscle has been approximated in a transverse manner. The skin may be closed with sutures of fine silk or clips, but we have obtained the best cosmetic results with a continuous subcuticular stitch of fine (No. 00000) Kaldermic suture material on an atraumatic needle. This stitch is removed in seven or eight days and the resulting hairline scar is almost invisible. If hemostasis has been adequate no drainage need be employed.

The technic described above is also used in the excision of a thyroglossal sinus. The tract must be followed upward, and even though a cord cannot be palpated, a complete block of tissue 5 to 7 mm. in diameter must be removed all the way to the base of the tongue, with the invariable excision of the central portion of the hyoid bone.

Patients with an exposed midline piece of mucous membrane, as shown in Figures 2 and 3, are extremely difficult to handle, principally because a vertical elliptical incision must be employed. In these cases it is again always advisable to remove a complete block of tissue to the base of the tongue. The vertical approximation of the platysma muscle and skin may give an excellent immediate cosmetic result, but these wounds have a great tendency to keloid formation and contracture.

A word of caution must be given concerning the removal of an ectopic thyroid gland which has been mistaken for a thyroglossal cyst. Such an accident has occurred in one case at this hospital (Fig. 11), and it is pertinent to record the lessons learned therefrom. To avoid such an unfortunate experience, two rules should be adopted. First, if there is any question about the cyst's containing solid tissue, it should be opened before completely detaching it from its bed. If it is found to contain thyroid tissue, it can be left in its abnormal position in the neck and the wound closed. Secondly, if high midline thyroid tissue is found, it should not be removed without ascertaining that a normally placed thyroid gland is also present. It will usually be found impossible to dissect down-

ward from the high neck wound in order to obtain this information; hence it is justifiable to make a small transverse midline incision 1.0 to 1.5 cm. long over the thyroid isthmus so as to expose and positively identify the thyroid gland. Making



FIGURE 11.

Operating-table photograph of a dissected specimen which was thought to be a thyroglossal cyst, but which later proved to be an ectopic thyroid gland. The child subsequently developed myxedema, necessitating administration of thyroid.

this second exploratory incision is far preferable to producing myxedema by blindly and unhesitatingly removing a high ectopic thyroid gland. It is seldom that these considerations must be borne in mind, but they should be remembered by anyone who treats thyroglossal-duct lesions.

RESULTS OF TREATMENT

Three of our cases were successfully treated by intraoral procedures, since the cysts presented in the mouth at the base of the tongue. Ninety-one cases were treated by the complete operative procedure, which included removal of the middle of the hyoid bone. None of these patients have had a recurrence. In 16 cases incomplete operative procedures were done, in which a portion of the hyoid bone was not removed or insufficient tissue was removed above the hyoid bone. Eight of these patients have shown no evidence of recurrence, but the other 8 have had subsequent formation of a cyst. Six of the recurrences were subjected to secondary or tertiary procedures before a final cure was obtained, and 2 patients refused

to have subsequent treatment. The 2 patients with a midline exposed mucous membrane have not had good cosmetic results, and because of these experiences we are convinced that such cases should have routine excision followed by x-ray therapy four to seven days after operation, in order to abolish or reduce keloid formation.

SUMMARY

The clinical findings from 198 children with thyroglossal cysts or sinuses are summarized. If a thyroglossal cyst is small, if disfigurement is minimal, and if inflammation has not occurred, surgical therapy may be omitted or deferred. If the cyst is large it should be removed in order to

improve the cosmetic appearance and to lessen the danger of the superimposed infection that is apt to follow. All thyroglossal-duct sinuses should be surgically removed because they are a source of recurring inflammatory disease.

Operative treatment should always include resection of the central part of the hyoid bone and also removal of a block of tissue upward as far as the base of the tongue. Less complete operation will often effect cures, but to ensure against recurrences the more extensive procedure should always be done. The results of treatment in 110 surgically treated cases are summarized.

300 Longwood Avenue

ECZEMA IN INFANTS AND YOUNG CHILDREN*

LEWIS WEBB HILL, M.D.†

BOSTON

ECZEMA in infants and young children may be caused by allergy to foods, to inhalants, to organic or inorganic contactants, to fungous or low-grade pyogenic infection, or to chemical or mechanical irritation. The clinical picture and, above all, the search for the etiologic factor are therefore complicated. It is probably true, however, that most cases develop on an allergic soil, and discussion will be confined to this group.

Typical allergic eczema, or "atopic dermatitis," as it is now often called, seldom begins before the age of three months. The clinical picture may be quite variable, for although the typical lesion is a small exudative papule, there may instead be diffuse erythema, macules, vesicles or even wheals, and added to these, crusts, pustules, fissures or ulcers, the result of secondary changes due to trauma or infection. As a rule the lesions of atopic dermatitis do not have sharp margins, and if nummular or serpiginous flat lesions with sharp margins are seen, and there is not much itching, the chances are that one is not dealing with atopic dermatitis. This does not always hold, however.

The diagnosis of atopic dermatitis in an infant is suggested by the character of the eruption and the severe itching, and may often be confirmed by positive skin tests. Normal infants may give a positive intracutaneous reaction for a short time after eating a new food: they do not give positive scratch-test reactions at any time, so that if

such a reaction is obtained one can be sure that the infant is allergic, and that the basis of the dermatitis, at any rate, is of that nature. It is not uncommon, however, for infection with yeast-like organisms or with ordinary pyogenic cocci to be superimposed on an atopic dermatitis, and ammonia dermatitis of the buttocks is also common in these infants, so that sometimes the skin lesions seen in one case may in reality represent two or three different diseases. It should be remembered that not all so-called "eczema" is atopic dermatitis, and that not all atopic dermatitis is due to food alone.

Treatment in the main is fairly but by no means entirely satisfactory; the baby can as a rule be made more comfortable, and the skin can be improved. Prompt and spectacular cure is, however, uncommon, although it can take place. A combination of immunologic and local treatment is much better than either alone. The immunologic treatment consists in determining by the history and skin tests the allergens to which the infant is sensitized, and removal of these from the diet or environment. It must be remembered, however, that not all positive skin tests are of etiologic significance: some infants are able to take with impunity foods to which they give positive tests; others are promptly improved or cured when some food to which they react is removed from the diet, and as promptly break out again when it is resumed. The differentiation between etiologic and non-etiological skin tests is one of the most perplexing and least understood questions in allergy. There can be no doubt that many infants are relieved of their dermatitis when certain foods.

*This and the two subsequent papers were presented at a meeting of the Section on Pediatrics at the annual meeting of the Massachusetts Medical Society, Boston, May 21, 1940.

†Associate in pediatrics, Harvard Medical School, visiting physician, Children's and Infants' Hospitals.

notably milk and wheat, are removed from the diet.

It is not at all uncommon, however, particularly in the severer cases with erythrodermia, to remove all foods to which there are positive skin reactions and yet to see no improvement whatever. There is a wide gap in knowledge here, which needs filling in before this disease can ever be really understood. It is quite true that it develops on an allergic soil—there can be no argument about that. The relation of specifically sensitizing allergens to the production of the dermatitis is quite another question. Sometimes the cause-and-effect relation is quite clear; many times it is not clear at all.

Most babies with atopic dermatitis give positive skin reactions to egg white. This is probably of no direct etiologic significance, for these babies are not eating egg, although some have thought that the egg antibodies fixed in the skin cells cause the dermatitis, without intervention of antigen. About two thirds of the egg-sensitive infants will be made violently ill if they eat it, or are sent into shock if it is injected parenterally; for about a third it is harmless, in spite of positive skin tests. The origin of this early sensitivity to egg is not entirely clear: the most commonly held view is that it takes place in utero.

Milk and wheat are the two most important allergens concerned in the production of atopic dermatitis in infancy. Positive scratch tests to milk are, however, not very common, and the intracutaneous test must often be used to demonstrate sensitivity. A positive scratch test is usually of etiologic significance; a positive intracutaneous test may or may not be.

In dealing with milk sensitivity in eczema, goat's milk or a milk-free food may be of value; in my experience evaporated cow's milk is not often so. The objection to goat's milk is that there are often crossed reactions between it and cow's milk, so that the infant may be as sensitive to the former as to the latter. The disadvantage of the milk-free foods, most of which are made of soybean flour, is that they sometimes cause bulky, loose bowel movements and irritated buttocks. If the formula is cooked in a double boiler for three quarters of an hour, this tendency is considerably lessened. The use of goat's milk and of milk-free foods in the dietetic treatment of infantile eczema is common. They sometimes do a great deal of good. Often, however, they do none whatever, for they are unfortunately used indiscriminately in all sorts of cases whether or not there is milk sensitivity, or even in patients whose dermatitis has nothing to do with allergy. They are

of possible benefit only in patients who have eczema because they are hypersensitive to cow's milk.

Wheat is the most allergenic of the cereals, and positive skin reactions to it in eczematous infants are usually significant. The present practice of feeding large amounts of wheat cereal to infants at an early age has probably increased the incidence of sensitization to wheat. It is very uncommon for any of the antirachitic oils to have an etiologic relation to eczema, and there is therefore rarely any need to omit oil from the diet as is so often done. Orange juice is somewhat likelier to cause trouble. Even if skin reactions to orange are negative, it is not uncommon for itching to be severer after taking it. Of the vegetables, peas and spinach are the most allergenic.

Sensitivity to environmental allergens is not so common in infants as it is in older children, but should be considered. Sensitivity to feathers is not uncommon, and it is well not to allow an eczematous infant to sleep on a feather pillow. Silk and kapok are occasionally causes of dermatitis.

Local treatment is essential in all cases. First and foremost, it must be remembered that the dermatitis must be given a chance to heal; it can never do so if there is continual rubbing and scratching. There is no method of restraint that is entirely satisfactory; aluminum mitts are fairly effective. Face masks I no longer recommend. A rectangle of cellophane taped to the part of the bed sheet underneath the head is valuable in preventing trauma due to rubbing. I am not in favor of oil baths: if there is not too extensive acute skin involvement there is no objection to a water bath twice a week, followed by very careful drying and powdering with plain talc.

Local treatment with salves and lotions varies so much for different individuals and for different types of eruption that it is impossible to discuss it satisfactorily in detail: its principles must be learned by experience. There are certain general rules, however, which should be mentioned. Salves, and lotions containing insoluble powders, are as a rule not desirable during the acute, weeping stage. Wet compresses of 2 per cent resorcin or tannic acid solution containing 2 per cent boric acid, 1 per cent aluminum acetate solution or a 0.05 per cent potassium permanganate solution are better. In most cases of acute dermatitis, such as that caused by poison ivy, after the weeping has been controlled one usually turns to some very mild protective salve, such as Lassar's paste or zinc oxide ointment. For atopic dermatitis in infants, crude-coal-tar ointment may often be used

with advantage at this stage, for the condition is more chronic than is acute contact dermatitis in adults, and there is more thickening. Some of the white-tar preparations on the market are fairly satisfactory, but in my experience none are so good as coal-tar ointment. While the latter is being applied the skin should not be exposed to bright sunlight, and it should never be employed if pyogenic infection is present.

Coal-tar ointment is so efficient in many cases that a tendency has developed among pediatricians to use it on almost all eczematous eruptions. This is a mistake; unless there is considerable thickening and scaling, milder preparations will often do better.

In older children sensitization to environmental allergens is of considerable importance, although it may not often be possible to incriminate any particular allergen. The role of house dust is of some interest, and inasmuch as it is the rule for these patients to improve while in the hospital in a relatively dust-free environment, and to relapse as soon as they go home, and since many of them show large intracutaneous skin reactions to house dust, it probably plays a part, and in not a few cases an important one. If house dust causes dermatitis it probably does so more often by inhalation than by outside contact.

Precautions against dust in the home are as essential for older children with eczema as they are for asthmatic patients. While hyposensitization to house dust has been widely practiced in the treatment of asthma, and is often of benefit, there is little information available to indicate its value in dermatitis, and what information exists is contradictory. The whole subject of desensitiza-

tion in atopic dermatitis is obscure, and needs additional investigation.

Most older children with eczema have positive skin reactions to a number of foods. Sometimes these are of etiologic significance, sometimes not; this makes difficult a correct evaluation of their presence. Sometimes the dermatitis is caused by a particular food and is cured when it is omitted; perhaps more often several or many foods are omitted without any benefit whatever, and the main cause of the dermatitis may be feathers or house dust, or it may be entirely unknown.

The question of what to omit from the diet, regardless of the skin reaction, is one that requires common sense. The skin tests, to be sure, are helpful, but if one is guided entirely by them and ignores other factors, such as the history and, in particular, careful local treatment, one will have little success. Atopic dermatitis should not be treated without regard to its immunological aspects; nor should it be treated on an immunological basis alone. It must be remembered also that in older children an eruption may have nothing whatever to do with the diet, or with the inhalation of any allergen. It may be due to contact with any one of a wide variety of chemical agents, such as dyes, medicaments and plant oils. Pediatricians in particular are inclined to forget this, because they have always been so interested in food and the digestive tract as the source of numerous ills in children.

There is still a great deal to learn about eczema. There is no sure or quick cure as yet, and to get the better of the disease will require time, patience and much careful investigation.

319 Longwood Avenue

THE PATHOLOGIC PHYSIOLOGY OF BRONCHIAL ASTHMA IN CHILDREN*

With Reference to the Role of Infection

HENRY N. PRATT, M.D.†

BOSTON

THE fundamental pathologic physiology of all atopic and anaphylactic phenomena is increased capillary permeability, smooth-muscle spasm and excessive mucus secretion. These three exaggerations of normal physiologic responses are present in varying degrees in both animals

and man. The amount in which any one is active depends on what tissue is involved. For example, in urticaria the primary lesion is increased capillary permeability; in guinea-pig anaphylaxis, smooth-muscle spasm of the bronchioles; and in human hay fever, excessive secretion of mucus associated with increased capillary permeability as evidenced by the pale, edematous nasal mucous membrane. In human allergy there is a fourth

*From the Department of Pediatrics, Harvard Medical School; and the Infants' and Children's Hospitals.

†Instructor in pediatrics, Harvard Medical School, assistant physician, Medical Services, Infants' and Children's Hospitals.

factor, the significance of which is not understood, namely, tissue and sometimes blood eosinophilia.

These four factors can be well demonstrated by examining pathologic tissue from asthmatic children. It is difficult to obtain such material, because death from uncomplicated asthma in childhood is relatively rare. There have been only four cases at the Infants' and Children's Hospitals in the last few years.

Figure 1 shows a gross specimen of lung. It

smooth-muscle coat of the bronchioles. This can be seen in Figure 2. Here will be noted an invagination or wrinkling of the mucous membrane due to spasm of the surrounding smooth-muscle coat. The picture is reminiscent of the anaphylactic guinea-pig lung. This spasm prevents the proper expectoration of the excessive mucus, which consequently dries, producing the plugs. Observation of these specimens explains clearly why the asthmatic child has so much difficulty in breathing during an acute paroxysm.



FIGURE 1. *Gross Section of Asthmatic Lung.*

Note the spongy appearance and the mucus plugs in the bronchi and bronchioles.

is spongy and fully expanded. Normally the lungs collapse when air is admitted to the pleural cavities, but asthmatic lungs hold their shape and actually remain overextended with air when removed from the chest. Small slices may be cut from the lung, and these too hold their shape instead of collapsing. This is due to two factors. First, the excessive mucoid secretions become dried and inspissated, producing hard, rubbery plugs that completely occlude the bronchioles and smaller bronchi. In the cross section of lung in the illustration this can be readily seen. The mucus plugs tend to stand up beyond the cut surface of the lung. If one grasps a plug with forceps and tries to pull it out, it resists. When released, it snaps back into place. The second factor tending to make the lung hold its shape is spasm of the

Further microscopic studies disclose a mild edema of the peribronchial spaces (Fig. 3). In many of these areas there are excessive numbers of eosinophils. Polymorphonuclear leukocytes are relatively rare, but here and there a group of them may be found, suggesting the presence of some infection, although it is not certain that they necessarily indicate infection. The mucous glands appear hypertrophied and overactive. The plugs of mucus with cellular elements and debris are visible in the lumens of the bronchioles and bronchi. A very characteristic finding is the thickening and hyalinization of the basement membrane of the bronchioles. The significance of this condition is unknown.

The entire pathology in the periphery of the lung is secondary to that in the bronchioles. Em-

physema with flattening and rupture of the alveolar walls is dependent on the ball-valve action of the mucus plugs, which permits the ingress of air during the expansion of the thoracic cavity in inspiration, but traps it behind the plugs during expiration. In other areas there is atelectasis where the mucus plugs have completely occluded the bronchioles, so that the air distal to the plugs is absorbed and the alveolar spaces collapse.

What is the significance of the occasional areas

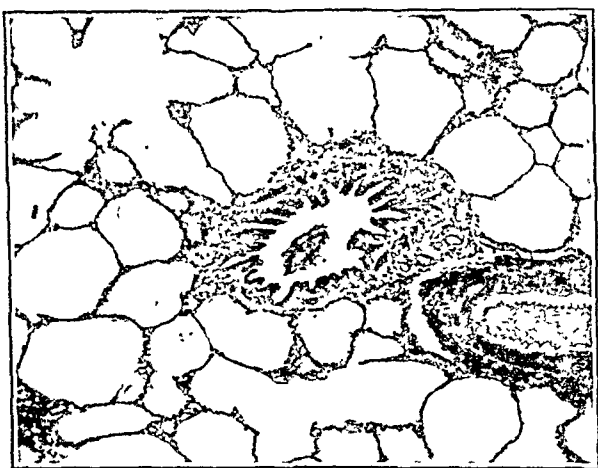


FIGURE 2. Section of a Constricted Bronchiole.

Note the resulting flattening and the rupture of the alveolar walls.

of infiltration with polymorphonuclear leukocytes? This brings up the question of infection and its role in the production of an asthmatic attack. At the outset it should be made clear that this question is not yet satisfactorily settled. However, among pediatricians dealing extensively with asthmatic children there is essential agreement.

The part played by infection may be divided into four categories: bacterial allergy; respiratory infections acting as a trigger mechanism; infections secondary to the asthmatic attack; and focal infection. It has often been predicated that a child may become sensitized to bacteria which he harbors somewhere in the respiratory tract. The classic example is pulmonary tuberculosis and the tuberculin reaction. This is certainly an allergic reaction. But asthmatic paroxysms due to sensitivity to the products of the tubercle bacillus are extraordinarily rare. In like manner a delayed, tuberculin-type skin reaction to a bacterium cultured from the respiratory tract of an asthmatic child or to one of its products can often be demonstrated, and undoubtedly means that the child has been infected with that organism. But, just as with tuberculosis, this type of sensitization to an organism is seldom responsible for asthmatic

seizures. The occasional satisfactory result following autogenous or stock vaccine therapy is in most cases due to shock and is entirely nonspecific.

Secondly, respiratory infections such as the common cold often precipitate asthmatic attacks in atopic children. In such cases the child is usually sensitive to some food or inhalant which he can tolerate except in the presence of infection. When he catches cold, some alteration occurs in the immunologic mechanism or respiratory mucous membrane so that he can no longer tolerate an extrinsic protein substance to which he is sensitive. This has been clearly demonstrated over and over again by abolishing the extrinsic factor; the child then has a cold without asthma. In these cases the respiratory infection may be considered as a nonspecific trigger mechanism.

Thirdly, infections may be secondary to an attack of asthma initiated by some extrinsic factor



FIGURE 3. Section of a Bronchiole Filled with a Mucus Plug.

Note the interstitial edema, the cellular infiltration, consisting mostly of eosinophils, and the hypertrophy of the mucus glands.

to which the child is sensitive. It is a common experience to see a child develop a typical attack of vasomotor rhinitis, often mistaken for a cold. Within a few hours he begins to cough and wheeze. The temperature, however, remains normal, and the pharynx shows no evidence of infection. After twenty-four hours fever and leukocytosis may appear. The infection that is suggested in the microscopic sections by the infiltrations with polymorphonuclear leukocytes probably began in the inadequately aerated portions of the lungs. The infection is entirely secondary. Such infection, once established, may produce a chronic irritation in the bronchi which causes the attacks of asthma to continue intermittently for several weeks. A good example of this is the patient with

ragweed asthma who begins to wheeze in late August when the air is laden with pollen. He is somewhat better in mid-October when the pollen has disappeared, but because of secondary infection he may continue to wheeze until Thanksgiving or even Christmas.

Fourthly, focal infection seldom plays a part in childhood asthma. In allergic children the lymphoid structures in the upper respiratory tract tend to hypertrophy, so that one is sorely tempted to remove the large, boggy tonsils and adenoids. Statistically it has been shown that removal of these structures has no lasting effect on the asthma. If the usual indications for removal of tonsils and adenoids are present, the operation should of course be performed, but asthma is definitely not one of the indications. Essentially the same principles apply in the management of sinuses. If they contain pus, they should be drained, and this sometimes temporarily relieves the asthma, but the presence of pus is rare in the sinuses of asthmatic children. The more usual

lesion is a thickened, hypertrophied mucous membrane. This is part and parcel of the allergic reaction, and such sinuses should be left strictly alone so far as operative intervention is concerned.

SUMMARY

The pathology of bronchial asthma is based on the fundamental physiology of atopic and anaphylactic phenomena. Increased capillary permeability produces edema; smooth-muscle spasm of the bronchioles holds the excessive mucus secretions so that they become inspissated and produce tenacious plugs which block partly or completely the smaller bronchi. This results in the formation of areas of emphysema and atelectasis. In the latter sites secondary infection may begin. In general, it may be assumed that infection is a sequela of the asthmatic attack, which is primarily based on an allergic reaction produced by extrinsic causes such as pollens, danders, dusts and foods.

319 Longwood Avenue

THE TREATMENT OF BRONCHIAL ASTHMA IN CHILDREN

ETHAN ALLAN BROWN, M.R.C.S. (LOND.) L.R.C.P.*

BOSTON

THE FACT that bronchial asthma is due to an increased capillary permeability, to smooth-muscle spasm and to excessive mucus secretion has just been stressed. Rational treatment would, of course, direct itself toward the correction of these abnormalities. However, since the cause of the condition is often an extraneous factor such as an inhalant or a food, correction may merely imply complete elimination of the causative allergen.

Treatment is best discussed under the following headings: symptomatic treatment, environmental control and general measures.

The acute attack in children can be treated by any of the sympathetico-mimetic drugs of the ephedrine group. Ephedrine sulfate is the best, and the usual dose is $3/8$ gr. It has undesirable side actions, and it is necessary that additional sedatives be given. The best of these is undoubtedly phenobarbital, since many of the barbiturates are vaso-spasmodic. It may be given in doses of $1/4$ or $1/2$ gr.

For the acute attack of greater severity, small doses of epinephrine (1:1000), 2 or 3 minims, may be injected subcutaneously, and are almost always specific. The dose can be repeated every fifteen minutes for four doses, if necessary. The average

dose given is larger than that needed, and very few children require more than 3 minims for relief.

It is not generally known that the oxidation of epinephrine in the system is delayed by the use of ephedrine at the same time. Ephedrine given by mouth will, in cases in which it is not necessarily effective by itself, enhance and prolong the action of the epinephrine.

Other remedies have been used for the acute attack, one of the most popular being syrup of ipecac, which causes nausea and vomiting, and owing to its expectorant action probably relieves the asthmatic spell. It is well to remember that for young children who cannot take a capsule, ephedrine can be put up in syrup form with phenobarbital; also, the capsule can be opened and the contents sprinkled on a teaspoonful of Karo or any other simple, palatable vehicle easily available. I have experimented with suppositories containing ephedrine and phenobarbital. The rectal medication seems effective in children who cannot take it orally.

In the severer cases, epinephrine in oil, 0.5 to 0.8 cc. of the usual preparation (2 mg. per cubic centimeter), should be given every twelve hours, with ephedrine given by mouth at the time of injection and six hours later. Status asthmaticus is not

*Instructor in medicine, Tufts College Medical School, consultant in allergy, Joseph H. Pratt Diagnostic Hospital

ACUTE HEPATITIS, JAUNDICE AND ABNORMAL BLEEDING AS COMPLICATIONS OF ACUTE APPENDICITIS WITH PERFORATION*

F. A. SIMEONE, M.D.,† AND JOHN D. STEWART, M.D.‡

BOSTON

FATALITIES following operations for acute appendicitis with perforation and peritonitis are usually the result of spreading peritoneal sepsis and its complications. Not uncommonly patients with prolonged intraperitoneal sepsis develop acute hepatitis, which may subside or progress to become a major factor in the patient's death. In these cases, the development of abnormal bleeding is a distressing sign, difficult to control and of grave prognostic significance.

Recent studies (Dam and Glavind¹; Stewart²; Stewart and Rourke³) have made progress in describing the nature of the hemorrhagic diathesis associated with jaundice from prolonged obstruction of the extrahepatic biliary passages. It has been shown that in most of these cases the abnormal bleeding is associated with a low plasma-prothrombin level. The evidence indicates that prothrombin is elaborated in the liver by an unknown process involving the participation of the fat-soluble vitamin K. An abnormally low concentration of plasma prothrombin may be due to a failure of vitamin K to reach the liver because of faulty intestinal absorption, as in obstructive jaundice, or to a failure of the damaged liver to elaborate the substance even in the presence of abundant vitamin K. Indeed, some cases of chronic obstructive jaundice present the problem of deficiency not only in absorption but also in liver function, so that both factors are operating to produce a low plasma-prothrombin concentration and the associated bleeding tendency.

The purpose of this report is to discuss two cases of intraperitoneal sepsis complicated by hepatitis and terminal bleeding.

CASE 1. J. B. T. (No. 353473), a 17-year-old boy, was admitted to the hospital because of low abdominal pain of 3 days' duration. During the 2 days prior to admission the pain had increased in severity and had become localized. Examination of the abdomen showed generalized tenderness and spasm, with maximal signs in the right lower quadrant. The temperature was 101.0°F. by rectum, the pulse 112, and the respirations 24. The white-cell count was 24,500, and urinalysis showed no abnormality.

*From the Surgical Laboratories of the Harvard Medical School at the Massachusetts General Hospital.

†Instructor in genitourinary surgery, Harvard Medical School; fellow in urology, Peter Bent Brigham Hospital.

‡Associate in surgery, Harvard Medical School; assistant surgeon, Massachusetts General Hospital.

Under spinal anesthesia operation was performed for acute appendicitis with perforation. Generalized peritonitis was found and *Escherichia coli* was subsequently cultured from the exudate. The appendix was removed, with drainage of the pelvis and right paravertebral gutter. On the first day after operation progress was satisfactory. Blood chemical studies revealed a hypoproteinemia and some reduction in the alkali reserve. The serum nonprotein nitrogen was 28 mg. per 100 cc., the serum chloride 96 milliequiv. per liter and the carbon dioxide combining power of the serum 35.9 vol. per cent. The serum protein concentration was 4.8 gm. per 100 cc. The patient was given a transfusion of 500 cc. of citrated blood.

On the evening of the 2nd postoperative day, jaundice was first detected in the scleras and bile was noted in the urine. By the following day the jaundice had deepened and a serum van den Bergh test showed a direct reaction, with 11.1 mg. of bilirubin per 100 cc. There had been no chills. The patient then showed clinical improvement and the jaundice began to clear, until by the 5th postoperative day the serum bilirubin was 6.5 mg. The temperature had fallen to normal. The next day, however, there was an abrupt rise in temperature to 103.2°F. by rectum, and from then on the patient's course was progressively downhill. The jaundice deepened again, until by the 9th postoperative day the bilirubin in the serum had risen to 12.6 mg. The same day there was bleeding from the wound amounting to about 300 cc. The bleeding continued the next day in spite of transfusions, the abdomen grew increasingly distended, and the patient became disoriented and delirious. A hematoma in the right paravertebral gutter was drained under local novocain anesthesia on the 10th postoperative day. Two days later the serum nonprotein nitrogen rose to 43 mg. per 100 cc., and the bilirubin to 21.4 mg. The patient died the next day, 13 days after operation. There had been some decrease in the bleeding from the wounds, but not complete cessation.

The significant abdominal findings at postmortem examination were generalized peritonitis and diffuse central necrosis of the liver. In addition there were found acute fibrinous pericarditis, acute pleuritis with pyohydrothorax, and *Esch. coli* and *Streptococcus faecalis* bacteremia. Jaundice was quite obvious at autopsy and was attributed to the hepatitis. The infected hematoma was found to have been well drained, but there was residual retroperitoneal sepsis, and the exudate was peculiarly hemorrhagic in character.

CASE 2. A. I. (No. 188575), a 13-year-old girl, was admitted to the hospital for treatment of acute appendicitis with perforation and spreading peritonitis. The temperature was 101.8°F. by rectum, the pulse 112, and the respirations 24. The white-cell count was 32,000, with 81 per cent polymorphonuclears, of which 5 per cent were "stab" forms. The urine was normal. Under ether anesthesia a gangrenous perforated appendix was removed through a right pararectus incision. The pelvis was drained by a cigarette wick through a stab wound in the right flank.

There was no evidence of localization of the peritonitis. Cultures of the exudate showed *Esch coli*, *Proteus vulgaris* and nonhemolytic streptococci.

Postoperatively the patient showed steady improvement until the 8th day, when after a brief, mild chill the rectal temperature suddenly rose to 105°F. There was a corresponding rise in the pulse and respirations. In the evening a trace of jaundice became detectable in the skin and scleras. Twelve hours later the serum bilirubin concentration was 49 mg per 100 cc. This increased the next day, 10 days after operation, to 59 mg. The reaction was biphasic.

An indwelling stomach tube was kept on constant suction, and an adequate fluid balance was maintained by means of venoclyses and transfusions. The jaundice temporarily decreased, although the patient's condition continued to fail. On the 13th postoperative day, bleeding from the appendectomy wound set in. There was a generalized oozing from the superficial granulations as well as from the depths of the wound. Packing was only partly successful in controlling the bleeding. Four transfusions, totaling 2000 cc of citrated blood, were given during the next 2 days, without appreciable effect on the bleeding tendency. Fifteen days after operation the plasma prothrombin concentration was down to 38 per cent of normal. Capsules of vitamin K and bile acids were given orally. During the same day, however, the patient began to have convulsive attacks, became comatose and died. Before death the serum nonprotein nitrogen had increased to 38 mg per 100 cc. The chlorides were 1048 milliequiv per liter, and the serum protein concentration 52 gm per 100 cc. The van den Bergh reaction was still biphasic, and the serum bilirubin concentration was 131 mg. Autopsy was not performed.

The postoperative courses in these cases showed remarkable general similarities. Both patients had generalized peritonitis secondary to a ruptured acutely inflamed appendix. Each showed initial improvement after operation, followed by relapse. Jaundice was observed early in Case 1, late in Case 2. Of particular interest is the fact that both patients terminally developed a hemorrhagic diathesis.

The jaundice in Case 1 was attributable to liver insufficiency. Although objective evidence is lacking in Case 2, the clinical course was so similar to that of Case 1 that it is reasonable to assume a similar cause for the jaundice. Plasma prothrombin studies were not done in Case 1, as the determination was not then clinically available. In Case 2, a severe hypoprothrombinemia was found (38 per cent of normal), and again it is reasonable to attribute the abnormal bleeding of Case 1 to a similar deficiency in plasma prothrombin.

Ample evidence has accumulated since Dam⁴ demonstrated a relation between abnormal bleeding and fat soluble vitamin deficiency, indicating that a failure in the absorption or utilization of vitamin K is responsible for the hemorrhagic diathesis in patients with obstructive jaundice. Such

patients have been found to have an abnormally low concentration of prothrombin in the plasma, with resultant inadequacy of the clotting mechanism. Just what part is played by vitamin K in the synthesis or activation of prothrombin is not known.

In the 2 cases described above, the abnormal bleeding was probably due to a disorder in the vitamin K content. Three possible explanations present themselves.

The postoperative diet may have been deficient in vitamin K. If this were the vital factor, however, it would seem that the deficiency would become apparent more frequently in surgical practice.

The absorption of vitamin K from the intestinal tract may have been impaired. In obstructive jaundice the impairment is due to lack of bile salts in the gastrointestinal tract, with a consequent decrease in the absorption of fat soluble substances. In general peritonitis, the decreased absorption might be due to the frequently associated enteritis.

The disturbed liver functions attending the hepatitis may have interfered with the normal reaction whereby vitamin K effects the liberation or activation of prothrombin in the liver.

The last of the above suggestions appears to be the most plausible. It fits with the report of Greaves and Schmidt,⁵ who found that in rats deficient in vitamin A, even though carotene was supplied in abundance parenterally, there was no evidence that vitamin A was elaborated in the presence of liver damage. It follows from this interpretation that in cases of abnormal bleeding, such as the two presented above, oral or parenteral administration of vitamin K is not nearly so effective as it is in those cases where the fault is primarily one of intestinal absorption rather than depression of liver function. In this group, vitamin K therapy should be actively supplemented by transfusion.

SUMMARY

Two cases are described to illustrate the syndrome of acute hepatitis and hypoprothrombinemic bleeding following operation for acute appendicitis with perforation. Such bleeding may result in serious blood loss and extension of infection. Plasma prothrombin concentrations should be determined in cases of peritoneal infection of gastrointestinal origin, and blood transfusions and parenteral vitamin K therapy should be given as indicated.

REFERENCES

1. Dam, H., and Glavind, J.: The clotting power of human and mammalian blood in relation to vitamin K. *Acta med. Scandinav.* 96:108-128, 1938.
2. Stewart, J. D.: Prothrombin deficiency and the effects of vitamin K in obstructive jaundice and biliary fistula. *Ann. Surg.* 109:588-595, 1939.
3. Stewart, J. D., and Rourke, G. M.: Control of prothrombin deficiency in obstructive jaundice by the use of vitamin K. *J. A. M. A.* 113:2223-2227, 1939.
4. Dam, H.: The antihæmorrhagic vitamin of the chick: occurrence and chemical nature. *Nature* 135:652, 1935.
5. Greaves, J. D., and Schmidt, C. L. A.: The utilization of carotene by jaundiced and phosphorus treated vitamin A deficient rats. *Am. J. Physiol.* 111:502-506, 1935.

REPORT ON MEDICAL PROGRESS

ORTHOPEDIC SURGERY

JOSEPH S. BARR, M.D.*

BOSTON

ALTHOUGH disabilities of the musculoskeletal mechanism have been recognized and treated since the earliest times, it is only in recent years that orthopedic surgery has been recognized as a specialty. Its growth has been phenomenal. The recent report¹ of the Research Committee of the American Orthopaedic Association gives some indication of the number, variety and scope of the various research projects being carried on throughout the United States.

Perhaps one of the most characteristic features of the specialty is the fact that operative procedures are not well standardized; for the relief of an orthopedic disability by operative means, there is usually more than one choice, and sometimes an embarrassingly large number of operative procedures from which the surgeon must choose. Textbooks on surgical technic become outmoded very rapidly, but two recent books^{2,3} on operative orthopedics are so well written and illustrated that they should prove invaluable to the general surgeon in selecting the proper operation for a given case.

INEQUALITY IN LEG LENGTH

A wide variety of conditions, congenital or acquired, affect epiphyseal growth and cause discrepancy in leg length. If the discrepancy is less than 5 cm., it can be compensated for by a raise on the heel of the shoe, but more than that amount requires an unsightly high sole. Equalization of leg length up to 5 to 8 cm. can be produced by leg-lengthening procedures. The most popular and effective of these is the one described by Abbott,⁴ in which after osteotomy of the tibia and fibula and lengthening of the tendo achillis, the bone fragments are gradually distracted by means of skeletal traction. This entails prolonged hospitalization and a certain amount of risk of delayed

or nonunion, sepsis, malalignment, joint disabilities and so forth; and although it still holds a place in the armamentarium of orthopedic surgery, it is definitely less popular than it was a few years ago. Leg-shortening procedures, in which the sound limb is operated on, sacrificing a predetermined amount of length of the femur, have become more popular in recent years and seem to be supplanting the lengthening procedures as the method of choice in adults.⁵ Growing children who have progressively increasing shortening of one leg may be treated by sympathectomy (lumbar ganglionectomy) in an attempt to stimulate epiphyseal growth by increasing the peripheral circulation of the extremity. This procedure seems to be particularly effective in cases of poliomyelitis, but it must be done before much shortening has occurred.

Epiphyseal arrest (epiphyseodesis) has been proposed by Phemister.⁶ It seems to be the best method thus far devised for equalization of leg length in children. The principle of the operation is simple. By placing bone grafts across one or more growing epiphyses of the longer leg, a premature union of the epiphysis and diaphysis is brought about, and the final leg length is less than it would normally have been. The epiphyses at the knee joint, particularly the femoral epiphysis, are most commonly used. The choice of time of operation and the number of epiphyses to be fused depends on a number of variable factors, too involved to be discussed here. The important point is that there are now effective methods for the equalization of leg length, and that every child with appreciable discrepancy in rate of growth of the lower extremities should be under the observation of a competent orthopedic surgeon.

ARTHROPLASTY

One of the most interesting and spectacular procedures of the orthopedic surgeon is the re-

*Instructor in orthopedic surgery, Harvard Medical School; assistant visiting orthopedic surgeon, Massachusetts General Hospital.

establishment of motion in ankylosed joints. Successful results have been recorded for years, particularly in the knee, hip and elbow. Most surgeons have relied on the interposition of a double layer of fascia lata between the newly formed joint surfaces. Although fascia-lata arthroplasty of the elbow and knee is successful in a fairly high percentage of cases, the procedure as applied to the hip has not become very popular because of the rather high incidence of re-ankylosis or of painful joints after the operation. Smith-Petersen⁷ after years of experimentation with various types of molds interposed between the acetabulum and the head of the femur has finally evolved a technic for arthroplasty of the hip which seems to give satisfactory results in a high percentage of cases. A vitallium cup is fitted loosely over the head of the femur. This metal seems to cause little or no tissue reaction and, apparently, may be left in situ for an indefinite period of time, allowing free gliding motion of the bony surfaces on either side of the cup. Careful selection of the operative cases, proper operative technic and meticulous attention to postoperative care are all still essential if successful results are to be obtained. Attempts are being made to use this same material in arthroplasties of other joints, and it is to be anticipated that a suitable technic may be evolved for various joints of the body.

NONABSORBABLE FIXATION MATERIAL

The trend toward the use of nonabsorbable suture material, particularly silk, in clean surgical cases is as pronounced in orthopedic surgery as it is in other branches of surgery. The incidence of postoperative infection seems to be definitely decreased, and better and stronger wound healing seems to occur where proper silk material is substituted for absorbable catgut sutures.

Within the last few years, two new nonabsorbable fixation materials have proved themselves to be of real aid to the orthopedic surgeon. Stainless steel in the form of bone plates, screws, Steinmann pins, Kirschner wires and flexible suture wire has practically displaced the previously used vanadium steel. The more recently introduced vitallium,⁸ an alloy of cobalt, molybdenum and chromium, containing no iron, has also become very popular. Its one drawback seems to be that it is not malleable and is made by casting, so that there is some tendency toward brittleness. Both these materials seem to be practically inert, causing no irritation of the body tissues, even when left in place over long periods of time.

LOW-BACK PAIN AND SCIATICA

Low-back disability continues to be one of the most important and difficult problems confronting the orthopedic surgeon. Recent medical literature contains many articles concerning various aspects of this question. Under the intensive study which is now being carried out, new concepts of the etiologic factors involved are being elucidated, and it is fair to say that real progress is being made in the diagnosis and treatment of low-back disability. It needs to be reiterated and emphasized that a long list of etiologic possibilities are present in any given case, and that the solution of the problem depends on the taking of a detailed history, which includes not only the details of the present disability but also an investigation of the past history and the general medical and social factors. The physical examination must include a general medical examination and a detailed examination of the back in the standing, sitting and lying positions. Various special diagnostic tests⁹ are a necessary part of this examination. Also necessary is a routine neurological check-up, which should include at least eliciting the usual reflex responses, a check on the superficial and deep sensory responses to appropriate stimuli and an estimate of the muscular strength in the lower extremities and trunk. With this information at hand, the physician can select the necessary x-ray and laboratory examinations, and when their results are known, can synthesize a working diagnosis and outline suitable therapy in the great majority of cases. The day when a pain in the back was usually referred to as "slipped sacroiliac" has drawn to a close.

Steindler^{10, 11} has pointed out that for clinical purposes it is useful to divide the factors responsible for low-back and sciatic pain into two major groups. In the first, the disability is due to direct pressure within the spinal canal on the sciatic nerve, the lumbar plexus or the cauda equina. This may be caused by tumor, protruded intervertebral disk, hypertrophied ligamentum flavum and so forth. The symptoms in the second group are due to strain or irritation of a "trigger point" in the low back, with secondary reflex sciatic radiation of the pain. In this group there is no direct pressure on or irritation of the sciatic nerve or its components within the spinal canal. The diagnosis depends on finding a point of local tenderness, on which pressure accentuates the reflex referred pain, and its release at least partial relief from the pain. Local infiltration of the tender area with novocain produces complete temporary abol-

ishment of the reflex pain, and in some cases brings permanent cure. Examination of Steindler's cases of reflex sciatica reveals that they fell into six major groups: the sacrospinalis syndrome, in which the tender area was localized in the region of the posterosuperior or posteroinferior iliac spine; the lumbosacral syndrome, in which the point of tenderness was in the midline at the lumbosacral junction or over the fifth lumbar spinous process; the gluteal syndrome, in which the tenderness was lateral to the posteroinferior spine in the region of the origin of the gluteus maximus muscle; the transversosacral syndrome, in which tenderness was found in the iliolumbar angle and was associated with sacralization of the fifth lumbar transverse process; the tensor-fasciata syndrome, in which the Ober¹² test was positive and there was tenderness over the fascia lata, usually between the iliac crest and the great trochanter; and the myofascial syndrome, in which the tenderness was not well localized, but was usually present over the erector spinae muscle groups on either side of the spinous processes of the lumbar vertebrae.

Anatomic variations in the formation of the lumbosacral skeleton are common, and in the past certain of these have been considered to be common causes of low-back and sciatic pain. The consensus at the present time seems to be that no one of these variations is inevitably followed by back disability, and that in many cases their presence as revealed by the x-ray is an incidental finding.

Spondylolisthesis, or forward displacement of the vertebral column consequent to a defect or solution in continuity in the neural arch of a vertebra, is present in 5 or 6 per cent of the general population. However, examination of 200 fetal skeletons failed to reveal a single case of this condition, and for this reason Batts¹³ thinks that the congenital-malformation theory is untenable. Hitchcock¹⁴ in a careful study of the vertebral ossification centers of 90 fetal spines also failed to find a single example of spondylolisthesis or of accessory ossification centers. He noted, as has Willis,¹⁵ the presence of an area of great potential weakness at the isthmus zone, and was able experimentally to produce fractures in this area with very little force by hyperflexion of the spine. He concludes that spondylolisthesis is due to birth trauma and is not a congenital anomaly. Recurrent or persistent lumbosacral backache, sometimes accompanied by radiation of pain down the posterior thighs, is the commonest symptomatology associated with spondylolisthesis, although Friberg¹⁶ found that 10 per cent of his patients had no

symptoms whatever, and that many of them were able to do heavy work. There are two available methods of treatment of this condition. The conservative method includes some type of support, such as a corset or brace, restriction of activities to within the limits of discomfort, and carefully graded exercises. If this procedure fails to relieve symptoms, or if there is evidence of increased displacement of the vertebra, operative fusion of the area is indicated.

RUPTURED INTERVERTEBRAL DISKS AND THICKENING OF THE LIGAMENTUM FLAVUM

In 1934 a paper was published by Mixter and Barr¹⁷ in which attention was called to the fact that posterior protrusion of intervertebral-disk tissue into the spinal canal occurred more frequently than had previously been supposed, and that the symptoms in such cases were often similar to those attributed to sacroiliac strain, that is, acute low-back pain accompanied by severe sciatic radiation. Interest in this subject has increased from year to year, and there have been several recent symposiums.^{18, 19} It now seems quite definitely established that one of the commonest, if not the commonest, causes of intractable sciatic radiation of pain unrelieved by the usual supportive measures is posterior protrusion of an intervertebral disk in the low-lumbar region pressing on one or more roots of the cauda equina. Although both sexes and almost all ages are affected, by far the majority of cases occur in vigorous men between the ages of twenty and forty-five. A history of an injury to the back while lifting a heavy weight or of a fall from a height is elicited in about half the cases. There may be a long history of relapses and remissions, with a final attack which is severe and unrelieved by any of the usual conservative methods of treatment. The pain characteristically radiates down the posterior thigh and the posterolateral calf to the ankle. On examination, abnormal flattening or actual reversal of the lumbar lordosis is noted, often with a list of the lumbar spine either toward or away from the affected side. All motions of the lumbar spine are restricted by muscle spasm, and there may be a point of local tenderness in the midline at the lumbosacral junction or just above it. Straight leg-raising on the affected side is as a rule markedly limited. Jugular compression may cause exacerbation of the radiating pain. A diminished or absent ankle jerk is the commonest neurologic finding. In addition, there may be areas of diminished sensation or anesthesia, usually of the lateral border of the foot or the outer aspect of the calf of the leg. In a few cases the lesion is so large as

to cause symptoms of paraplegia. The protein content of the cerebrospinal fluid is usually elevated, but a small percentage of cases give perfectly normal cerebrospinal-fluid findings. Routine x-ray examination may reveal some narrowing of the fourth or fifth lumbar intervertebral disk, but an absolute localization and diagnosis of this lesion cannot be made except by roentgenologic examination after the injection of a contrast medium. The use of air or oxygen (pneumomyelography) has been advocated by Chamberlain.²⁰ Other roentgenologists, particularly Camp²¹ and Hampton,²² have advocated Lipiodol. An accurate localizing diagnosis can be made with Lipiodol in over 90 per cent of cases, but the use of this contrast medium is not without some hazard, and it should be reserved for those cases in which the diagnosis cannot be made otherwise and in which surgery is necessary, so that the Lipiodol can be removed at the time of the laminectomy.

The treatment of ruptured intervertebral disk consists in laminectomy and removal of the extruded fragments. This gives relief of symptoms, often in a very dramatic fashion, in about 90 per cent of cases. The final results seem to be somewhat better if the operative area is strengthened by a spine fusion done at the same time the laminectomy is performed.

It has been demonstrated by Schmorl²³ and more recently by Horvitz²⁴ that posterior intervertebral-disk protrusions can be demonstrated by routine autopsy examination in a fairly high percentage of cases, apparently never having caused clinical symptoms. There is also a good deal of evidence to show that the acute symptoms of a certain percentage of the clinical cases may subside or disappear completely under conservative treatment. The most effective method of conservative treatment seems to be immobilization of the lumbar spine in a plaster cast, applied with the lumbar spine in a position of flexion. If this fails to give relief within a few weeks, operative removal of the protruded disk should be undertaken.

Thickening of the ligamentum flavum as the cause of low-back and sciatic pain has been mentioned in a previous progress report.²⁵ It is much less common than protrusion of the intervertebral disk, and the two lesions may occasionally be associated. The symptoms and signs of the two entities are very similar.

234 Marlboro Street

REFERENCES

- 1 Research Committee of the American Orthopaedic Association Orthopedic research in North America | Bone & Joint Surg 22 752 758, 1940
- 2 Steindler, A *Orthopedic Operations Indications technique and results* 766 pp Springfield Illinois Charles C Thomas 1940
- 3 Campbell W C *Operative Orthopaedics* 1154 pp St Louis C V Mosby Co., 1939
- 4 Abbott L C, and Saunders J B : Operative lengthening of the tibia and fibula Preliminary report on further development of principles and technic *Ann Surg* 110 990-991, 1939
- 5 Wilson, P D, and Thompson T C A clinical consideration of the methods of equalizing leg length *Ann Surg* 110 992 1015, 1939
- 6 Phenister, D B Operative arrestment of longitudinal growth of bones in the treatment of deformities | Bone & Joint Surg 15 115, 1933
- 7 Smith Petersen, M N Arthroplasty of the hip new method | Bone & Joint Surg 21 269 285 1938
- 8 Wearable, C S, and Suggs G Vitalium nails in fractures of the hip *Surg Gynec & Obst* 70 964-965, 1940
- 9 Ellis J D Examination of the injured back *Am J Surg* 42 561 576, 1938
- 10 Steindler, A Differential diagnosis of pain low in the back allocation of the source of p.in by the procaine hydrochloride method | *J Am Mt* 110 106-113 1938
- 11 Idem The interruption of sciatic radiation and the syndrome of low back pain *J Bone & Joint Surg* 22 28 34 1940
- 12 Ober, F R Relation of the fascia lita to mechanical disabilities of the spine *Surgery* 4 21 32, 1938
- 13 Batts M The etiology of spondylolisthesis | Bone & Joint Surg 21:879 884 1939
- 14 Hitchcock, H H Spondylolisthesis observations on its development, progression, and genesis | Bone & Joint Surg 22 1 16 1940
- 15 Wilkerson, A The separate neural arch | Bone & Joint Surg 13 709 721, 1931
- 16 Friberg S Studies on spondylolisthesis *Acta chir Scandinav Supp* 55 I 140 139
- 17 Mixer, W J, and Barr, J S Rupture of the intervertebral disc with involvement of the spinal canal *New Eng J Med* 211:210 215 1934
- 18 Walsh, M N Clinical and neurological aspects of low back and sciatic pain *Radiology* 33 681-687, 1939
- 19 Love I G, Spurling, R G, Granitham E G, Saunders J B Inman, V T Stokeye, B, Macy, H B, Hampton, A O, Walsh M N, Galloway, J D B, Broders A C, and Ghormley, K C Symposium of protruded intervertebral discs *Arch Surg* 40 373 538 1940
- 20 Barr, J S, Smith, A Def, Ober, T R, and Mitchell, J I Symposium on Intervertebral Disks *Surg* 4 14 1938
- 21 Chamberlain, W E and Young B R The diagnosis of intervertebral disc protrusion by intraspinal injection of air air myelography | *J Am A* 113 2022 2024, 1939
- 22 Camp, J D The roentgenologic diagnosis of intraspinal protrusion of intervertebral disks by means of radiopaque oil | *J Am A* 113 2024 2029 1939
- 23 Hamilton, A C and Robinson, J M The roentgenographic demonstration of rupture of the intervertebral disc into the spinal canal after the injection of lipiodol " " " " "
- 24 Schmoll G Ueber knorpelige Bandscheiben Fortsch r d " " " " "
- 25 Horwitz, T Lesions of the intc " " " " "
- 26 The lumbar vertebrae an anatomic study of seventy five human cadavers *Surg* 4 140 425 1939
- 27 Adams, J B Report on medical progress clinical neurology *New Eng J Med* 223 376-380, 1940.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 26421

PRESENTATION OF CASE

A sixty-two-year-old physician entered the hospital complaining of increasing dyspnea and edema of three and a half months' duration.

The patient stated that his systolic blood pressure had been between 160 and 170 for many years and that he had had an occasional twinge of apical non-radiating cardiac pain, lasting but a few minutes and usually brought on by emotion. Five years before admission he had an acute attack of severe precordial pain, and an electrocardiogram at that time indicated a posterior occlusion. He remained in bed for one month thereafter and then returned to work, with no untoward effects until one year before entry. At that time he exerted himself unduly, and this indiscretion was followed by marked dyspnea, cough and bloody sputum. These symptoms all cleared with rest. Nine months before admission he was digitalized, put on a maintenance dose of 0.1 gm. daily and carried on until four months before entry, when he noticed the gradual onset of increasing nausea, anorexia and dyspnea. One month before admission the digitalis was discontinued in a partially successful attempt to control the nausea, with the result that peripheral edema developed and dyspnea finally prevented him from lying down.

His past illnesses and family history were irrelevant.

Physical examination showed a sallow, dyspneic, man who coughed frequently and complained of pain in the right chest. The neck veins were pulsating slightly. The heart borders were percussed 3 cm. from the midline on the right and 11 cm. on the left; the supracardiac dullness was 6 cm. in breadth. The rate was rapid, with a gallop rhythm and an auscultatory pulsus alternans at 118 to 130 systolic, 80 diastolic. In addition there was a high-pitched murmur, which was thought to be diastolic but which was impossible to time accurately because of the rapid heart rate. The lung bases were dull to percussion, with moist rales and distant breath sounds on auscultation. There was also a slight right axillary friction rub. The tender liver was palpated two

fingerbreadths below the costal margin, and there was an abdominal fluid wave and shifting dullness. There was pitting edema of the legs, extending up to the mid thighs, and in the sacral region.

The temperature was 100.4°F., the pulse 120, and the respirations 28.

Examination of the urine was negative. The blood showed a red-cell count of 4,700,000 with a hemoglobin of 85 per cent, and a white-cell count of 27,400 with 90 per cent polymorphonuclears. The nonprotein nitrogen of the blood was 58 mg. per 100 cc.

The patient was treated with digitalis and diuretics, but at no time did he respond favorably, although his peripheral edema decreased. Three weeks after admission, his temperature rose abruptly and he coughed up bloody sputum. He gradually became disorientated, developed a pleuropericardial friction rub and died one month after admission.

DIFFERENTIAL DIAGNOSIS

DR. SYLVESTER MCGINN: If we have all the information available on this patient,—and I assume that we have,—we should be able to make an adequate diagnosis. The first clue to possible etiology of the illness is the story of a systolic blood pressure of 160 to 170 for years. The corresponding diastolic pressures are not mentioned, and the only complete reading noted was 118 to 130 systolic, 80 diastolic. Because the blood pressure was obtained when the patient was critically ill and in failure, we cannot say much about it. I think the systolic pressures of 160 to 170 do bring in a certain hypertensive factor. The next possible etiological clue is the story of occasional twinges of an apical, non-radiating cardiac pain, which came on with emotion and which lasted only a few minutes. This history alone does not justify a diagnosis of angina, but fortunately we can confirm involvement of the coronary vessels from the next sentence, which states that there was an acute attack of severe chest pain and electrocardiographic evidence of posterior coronary occlusion. That is definite. No other evidence brought into the abstract suggests any further coronary attacks. Yet if this man had one right coronary occlusion five years before he died, I should not be surprised if at postmortem he showed additional coronary involvement. It is impossible to localize it as to time.

It is interesting that the patient lived for five years with cardiac infarction and was an active physician, and that only one year before death did congestive failure begin to appear, although he

had apparently taken only one month's rest after the acute coronary attack. The symptoms of cardiac failure—shortness of breath, cough and bloody sputum—sound like more than paroxysmal attacks of cardiac asthma, for the description does not suggest that they were paroxysms with asthmatic wheezes coming at night. Moreover, it seems a farther advanced process—pulmonary edema with bloody sputum. These symptoms all cleared with rest. That brings up an important point in the treatment of this case. The patient was digitalized and put on a maintenance dosage, but no reference is made as to whether he also had diuretics at that time; it is just as important to treat early signs of left ventricular failure with diuretics as it is to use them later, when there is evidence of peripheral edema and anasarca. I think perhaps it is even more important, because you can hope to accomplish more with them and keep the patients free from symptoms of cardiac asthma for some time. As a matter of fact, in the cases of cardiac asthma looked up here, the average duration of life, once it appeared, was 1.6 years. In another series the average duration of life was 2.4 years. I believe that in the latter the improvement was due to the use of diuretics in addition to digitalis.

The digitalis was omitted in a partially successful attempt to control nausea and anorexia. The patient had been having increased dyspnea, and I suspect that a good part of the anorexia and nausea was due to increased congestion, rather than being dependent solely on the use of digitalis. Anorexia, nausea and all gastric disturbances are extremely common symptoms of congestion in any cardiac case.

The next thing leading to a diagnosis is the pain in the right chest, and later on we find that the patient had a moderate right axillary friction rub. It makes little difference whether it was slight or not; it was a definite finding, and I think the most logical explanation is pulmonary infarction. In the terminal illness there is another reference to a pleuropericardial rub, which may have been evidence of a pulmonary infarct on the other side. If you have one embolus the chances are that you are going to have another. The patient had a temperature of 100.4°F. This is important because Drs. Kinsey and White* have pointed out that any time a patient with congestive failure has an increase in temperature there should be some reason for it, and that the commonest cause of febrile reaction in congestive failure is pulmonary infarction.

The neck veins were pulsating slightly, a finding which is consistent with failure of the right

ventricle. There was evidence of increase in heart size, with the left border 11 cm. from the midline, and also gallop rhythm and auscultatory pulsus alternans. Pulsus alternans and gallop rhythm indicate left ventricular dilatation, and imply a very serious prognosis. One cannot say much about the high-pitched murmur that was impossible to time because of a rapid heart rate. It is not fair to make the diagnosis of valvular deformity on that description alone. In congestive failure with dilatation, it is not uncommon to hear systolic murmurs, oftentimes due to distention and dilatation of the mitral ring. I believe that if it was the systolic murmur of aortic stenosis the description would be more definite. The patient had evidence of right-sided heart failure—pitting edema to the thighs, ascites and a palpable liver. In other words he had left ventricular failure, followed by evidence of right-sided failure.

Examination of the urine was negative. Yet we later have the finding of a nonprotein nitrogen of 58 mg. per 100 cc., which I believe was probably due to the congestion. If there had been any considerable nephritic damage, the patient would not have had a normal urine. The white-cell count of 27,400 is high for uncomplicated pulmonary infarction, and rather high for phlebitis. There is no evidence of where the emboli originated. Often in cardiac cases we never do find where they started. They did not come from an intramural thrombus, because the only evidence of an acute coronary occlusion had occurred five years previously. I believe the congested veins became thrombosed at some point, as they very frequently do.

The terminal illness is not unusual, and yet it is of some interest. In spite of active treatment,—digitalis and diuretics,—the failure increased; this means that the heart muscle was beyond the point of being helped by rest or treatment. It is a fact, too, that when we do find pulmonary infarction in cardiac cases they are very resistant to digitalis or any other kind of therapy. Three weeks after admission and one week before death, the patient's temperature rose abruptly, and he coughed up bloody sputum. The sudden rise in temperature may have meant further infarction, or a pneumonic process. He became disorientated and developed a pleuropericardial friction rub. Were there any other determinations of the nonprotein nitrogen?

DR. HOWARD B. SPRAGUE: The nonprotein nitrogen was 22 mg. per 100 cc. on admission.

DR. MCGINN: Do you know when it changed to 58 mg.?

DR. SPRAGUE: A week before he died.

DR. MCGINN: He was admitted with a non-

*Kinsey, D., and White, P. D.: Fever in congestive heart failure. *Arch. Int. Med.* 65:143-170, 1940.

protein nitrogen of 22 mg., which later rose to 58 mg.; I presume the increase was dependent on the increasing congestion, because he apparently came in with properly functioning kidneys. The pericardial rub was probably not uremic in origin.

To make a final diagnosis, I am not sure of the hypertensive factor, but everything seems to fit in with it, especially the heart size and the story of an elevated systolic pressure. I should like to make a diagnosis of hypertensive arteriosclerotic heart disease, with an old posterior coronary occlusion,—there may have been other evidence of coronary disease, but this was the only definite occlusion,—cardiac hypertrophy and dilatation, especially of the left ventricle, congestive heart failure, first left-sided and later right-sided, multiple pulmonary infarction and terminal bronchopneumonia.

DR. SPRAGUE: The patient was taken care of by one of his confreres. I saw him in consultation several times, but he managed most of his own therapy. He was a very apprehensive individual, who gave up a good deal of his practice after he had had the cardiac infarct, but I was impressed at each examination how abnormal his heart remained, with poor sounds and with persistent gallop rhythm. Fluoroscopically the heart was apparently generally dilated and the pulsations were poor. He took digitalis, became nauseated, failed increasingly, omitted the digitalis and got into a vicious circle so that it was necessary to give diuretics. His physician preferred to have him in the hospital here. The diagnosis made was the one that Dr. McGinn has suggested, with one modification. The peripheral edema decreased with therapy, and the week before he died he was almost free from edema, which shows again that cardiac patients now die from infection and infarction rather than from dropsy. That observation has been made before and makes one question just how much good is accomplished by strenuous diuretic therapy, except from an esthetic standpoint. I also brought up the question as to whether the pericardial rub was uremic in origin. I said that it might be, only because of the rise in the nonprotein nitrogen. As Dr. McGinn has said, one of the things that make cardiac patients fail and resist all therapy is multiple pulmonary infarction, which I thought was present in this case.

CLINICAL DIAGNOSES

Coronary heart disease.
Pulmonary embolism.

DR. MCGINN'S DIAGNOSES

Hypertensive arteriosclerotic heart disease.
Coronary occlusion, old, right, with posterior myocardial infarction.
Cardiac hypertrophy and dilatation.
Congestive failure, right-sided and left-sided.
Pulmonary infarction, multiple.
Bronchopneumonia (terminal).

ANATOMICAL DIAGNOSES

Cardiac infarction, healed.
Cardiac aneurysm.
Mural thrombus, left ventricle.
Arteriosclerosis, marked, aortic and coronary.
Pulmonary infarction, multiple, bilateral.
Thrombosis, deep veins of left lower extremity.
Hydrothorax, bilateral.
Hydropericardium.
Peripheral edema.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: This is a postmortem roentgenogram showing the large number of pulmonary infarcts that this patient had. There were seven in all. One of the infarcts in the left lower lobe was adherent to the pericardium, and I believe that the friction rub was produced by the resultant pleuropericarditis. The deep veins of the left leg were the source of the emboli. There were 750 cc. of straw-colored slightly hemorrhagic fluid in each pleural cavity, 200 cc. in the pericardium and moderate edema of the legs—definite evidence of heart failure. The heart weighed 615 gm. and before opening showed an aneurysm of the left ventricular wall, undoubtedly the site of the infarct that he had had five years before entry. When the heart was opened, the wall of the aneurysm was quite thin, gray-white and fibrous, and involved the apex and the lower half of the interventricular septum. Superimposed on its endocardial surface was an old laminated mural thrombus, 2 to 3 cm. in diameter. There was no evidence of recent infarction. All the coronary arteries were markedly sclerotic and calcified, the lumens being about one fifth of the normal caliber. There was no fresh occlusion. The kidneys weighed 500 gm. and showed practically no vascular disease, an unusual finding in a man of sixty-two.

DR. SPRAGUE: A pleuropericardial friction rub is not uncommon in patients with pulmonary infarct, and we have found it a helpful point in confirming the diagnosis of deep infarcts with the pleural reaction at the mediastinal surface.

CASE 26422

PRESENTATION OF CASE

A seventy-three-year-old retired postman entered the hospital complaining of abdominal pain and diarrhea of ten days' duration.

Because of the patient's disorientation, the history was obtained from his son. Three years before admission the patient had suffered from an attack of chest pain and prostration. This attack was not associated with cough or dyspnea, nor had his ankles ever become swollen. Three similar attacks had occurred during the next three years, and his physician had kept him constantly digitalized. Ten days before entry he suddenly became disorientated, fell to the floor and lost motor co-ordination. He was put in a chair and sat there all day, unable to speak plainly or to hold a teacup. Motor co-ordination improved in twenty-four hours, and speech and rationality returned, although his memory seemed to have suffered appreciably. During the next week his muscular co-ordination and mental faculties showed still further improvement. Four days before admission he had abdominal pains, diarrhea and a temperature of 102°F. The abdomen became very tender, but was not distended. The stools were black, but contained no gross blood. The next day the temperature returned to normal, but the diarrhea continued. The day before entry the temperature was 101.5°F., and he went to stool frequently, but passed nothing.

In the past the patient had had scarlet fever complicated by mastoiditis that had resulted in deafness of the right ear. He was said to have been paralyzed in the right side for an unstated period, and his speech had become seriously impaired after a "shock" one year before entry.

Physical examination showed that the patient was undernourished, pale and acutely ill. Numerous areas of senile keratosis were present on the arms and hands. The mouth was dry, and the tongue coated. The heart did not appear to be enlarged. There were no murmurs, but there was complete arrhythmia; the sounds were of poor quality. The apex rate was 168, and the radial pulse 144, with a pulsus alternans. The blood pressure was 154 systolic, 76 diastolic. Resonance and breath sounds were diminished on the left, and a peculiar type of cogwheel tubular respiration was heard over the left second and third interspaces. There was generalized abdominal tenderness, but no masses could be felt.

The temperature was 103.6°F., and the respirations 35.

Examination of the urine showed a ++ test for

albumin. Examination of the blood showed a red-cell count of 5,030,000 with a hemoglobin of 17.2 gm. (photoelectric-cell technic), and a white-cell count of 26,700. The nonprotein nitrogen of the blood serum was 35 mg. per 100 cc., and the carbon-dioxide combining power 24.6 vol. per cent. A blood Hinton test and a blood culture were negative. The sputum contained Type 9 pneumococci. Examination of the stools was negative on two occasions.

X-ray films of the chest, taken with a portable machine, were negative. Similar films of the abdomen showed no dilatation of the small bowel or colon; several gas-filled loops of bowel were present in the pelvis. There were no abnormal soft-tissue masses.

On the second hospital day the patient's abdomen was somewhat distended, and there were deep tenderness and slight muscular spasm in the right lower quadrant. Peristalsis appeared to be increased. Rectal examination at this time revealed a mass above the prostate, which was firm, tender and more pronounced on the left side. A steadily rising white-cell count had reached 39,700. He was treated expectantly, and eight days later the mass was larger and equally distributed on both sides. One examiner noted the presence of blood and mucus on the rectal glove, but an examination of the stools, recorded two days later, was negative. The white-cell count rose to 47,700. The patient began to go downhill, becoming weaker and unable to retain fluids by mouth. The cough increased in severity, and rales were heard at the left lung base. On the fifteenth hospital day the mass palpated by rectum had reached even greater proportions, and the center seemed somewhat softened. The patient's condition was considered too critical to attempt surgery, and he died three weeks after admission.

DIFFERENTIAL DIAGNOSIS

DR. RICHARD H. WALLACE: We have an old, disorientated man whose history, obtained from his son, included four attacks of chest pain and prostration during the previous three years. In addition, a year earlier he had had a "shock," with right hemiplegia, which apparently disappeared, and ten days before admission another vascular accident of some sort from which he partially recovered.

On admission he had a rapid, weak pulse with complete arrhythmia, so that there was not much question that he had severe cardiovascular disease. This complicates the picture somewhat. In addition, he had a productive cough, rapid respirations and increasing signs in the chest. Our problem is to try to diagnose the lesion in the abdo-

The New England Journal of Medicine

Formerly the
Boston Medical and Surgical Journal
Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE
ON PUBLICATIONS

Official Organ of
THE MASSACHUSETTS MEDICAL SOCIETY
THE NEW HAMPSHIRE MEDICAL SOCIETY
THE VERMONT STATE MEDICAL SOCIETY

EDITORIAL BOARD

Joseph Garland, M.D.	John P. Sutherland, M.D.
William B. Breed, M.D.	Stephen Rushmore, M.D.
George R. Minot, M.D.	Henry R. Viets, M.D.
Frank H. Lahey, M.D.	Robert M. Green, M.D.
Shields Warren, M.D.	Charles C. Lund, M.D.
George L. Tobey, Jr., M.D.	John F. Fulton, M.D.
C. Guy Lane, M.D.	A. Warren Stearns, M.D.
William A. Rogers, M.D.	Dwight O'Hara, M.D.

ASSOCIATE EDITORS

Thomas H. Lanman, M.D.	Donald Munro, M.D.
Henry Jackson, Jr., M.D.	
Walter P. Bowers, M.D., EDITOR EMERITUS	
Robert N. Nye, M.D., MANAGING EDITOR	
Clara D. Davies, ASSISTANT EDITOR	

SUBSCRIPTION TERMS: \$6.00 per year in advance, postage paid, for the United States; Canada, \$7.04 per year; \$8.52 per year for all foreign countries belonging to the Postal Union.

MATERIAL for early publication should be received not later than noon on Saturday.

THE JOURNAL does not hold itself responsible for statements made by any contributor.

COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston, Massachusetts.

CO-ORDINATING MEDICAL- PREPAREDNESS COMMITTEE

OFFICIAL action has finally been taken whereby a co-ordinating committee for medical preparedness has been appointed. This committee, known as the Health and Medical Committee, is a subordinate body to the Council of National Defense, and is composed of the following: Dr. Irvin Abell, of Louisville, Kentucky, chairman; Dr. Lewis H. Weed, of Baltimore; Surgeon General Magee, United States Army; Surgeon General McIntire, United States Navy; and Surgeon General Parran, United States Public Health Service. Since Dr. Abell is chairman of the Committee on Medical Preparedness of the American Medical Association, and Dr. Weed, chairman of the Division of Medical Sciences of the National Research Council, it is difficult to conceive how a better selection of personnel could have been made. The

committee is empowered to appoint various subcommittees to furnish information and advice in regard to special problems, and many of these subcommittees are already functioning.

The committee is specifically authorized "to advise the Council of National Defense regarding the health and medical aspects of national defense and to co-ordinate health and medical activities affecting national defense." In exercising this authority it may request the aid of the laboratory, equipment and advice of the medical departments of the Army, Navy and Public Health Service, and may enter into contracts with and transfer available funds to these departments, as well as with or to individuals or educational and scientific institutions, for studies, investigations and reports.

The appointment of a co-ordinating committee rather than a co-ordinator appears to have been a wise move, for, as pointed out in the August 8 issue of the *Journal*, "the responsibilities [of medical preparedness] seem to be too varied and too great to be shouldered by any one individual." With the committee constituted as it is, the medical profession and the country at large can be assured that the problems of medical preparedness will be handled wisely and expediently.

SALVATION ARMY APPEAL

As in previous years, a group of public-spirited men and women of the business world are leading the Greater Boston Annual Maintenance Appeal of the Salvation Army. The drive, which began on October 7 with a dinner at the Boston City Club, will last until November 9.

The campaign organizations in the corps cities of Cambridge, Chelsea, Everett, Malden, Medford and Somerville will raise \$25,000 of the \$200,000 that represents the Salvation Army's goal for 1940-1941. A quota of \$38,000 will be assigned to the thirty-one towns of Greater Boston where no corps organizations exist.

The amount to be collected is an increase of \$5000 over the quota set last year. The money will pay for the maintenance of more than thirty institutions that serve the needy.

This is indeed an appeal, a request for support

of an organization that has done such splendid and unselfish work among the less fortunate members of the community. Because physicians in particular recognize the value of the Salvation Army's services, they will undoubtedly be the first to respond.

MEDICAL EPONYM

ECK'S FISTULA

Nikolai Vladimirovich Eck (b. 1849) of St. Petersburg (now Leningrad), published a "preliminary communication" in the *Voyenno-Meditsinsky Journal* (130:1, 1877) entitled "K voprosu o pervyazkie vorotnoi veni [Ligature of the Portal Vein]." A portion of the translation follows:

If in the dog, after establishing a free communication between the inferior vena cava and the portal vein, one ties off the portal vein, the change in direction of the blood flow and the deprivation of the liver of blood from the portal vein produce no serious results in the organism. The animal recovers from the operation, his nutrition improves after recovery, and he remains in perfect condition

The technic of the operation is described and its possible application to the treatment of human ascites mentioned.

The medium by which this experimental procedure attained its first wide publicity was an article entitled "Die Eck'sche Fistel zwischen der unteren Hohlvene und der Pfortader und ihre Folgen für den Organismus [Eck's Fistula between the Inferior Vena Cava and the Portal Vein and Its Results upon the Organism]" by Hahn, Massen, Nencki and Pavlov, which appeared in the *Archiv für Experimentelle Pathologie und Pharmakologie* (32:161-210, 1893).

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

RAYMOND S. TITUS, M.D., Secretary
330 Dartmouth Street
Boston

THE MATERNAL MORTALITY STUDY IN MASSACHUSETTS FOR 1939

This is the third year that the Section of Obstetrics and Gynecology of the Massachusetts Medical Society has carried on an investigation of

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

maternal mortality. It is to be continued through 1941. Two hundred and fifty-five cases were reviewed during 1939, and of these, 2 were found to be nonpuerperal, giving a total of 253 puerperal deaths. The maternal death rate for 1939, 3.4 per cent per 1000 live births, as given by the Massachusetts Department of Public Health, is very encouraging when compared with the rates for 1937 and 1938, which were 4.1 and 3.7 per cent respectively. A comparative analysis of the puerperal causes of death for the past three years is as follows:

CAUSE OF DEATH	No OF DEATHS		
	1937	1938	1939
Sepsis (including septic abortions)	111	66	74
Medical deaths (pneumonia, cardiac disease, chronic nephritis and so forth)	57	54	57
Embolus	32	28	23
Hemorrhage (including separated placenta and placenta previa)	30	36	36
Albuminuria and eclampsia	29	31	32
Accidents of labor	13	6	8
Abortions (not septic)	9	3	4
Surgical deaths	10	13	5
Anesthesia	6	9	4
Ectopic pregnancy	6	12	5
Transfusion	3	2	3
Shock	3	7	2
Fernicious vomiting	4	5	
Sudden death	2		
Dystocia, with acute dilatation of heart		1	
Suicide		2	
Mesenteric thrombosis		1	
Totals	315	276	253

Sixty-seven autopsies were obtained in 1939, a percentage of 23; this is an improvement, but an even greater number should be performed.

Sepsis was still the greatest cause of mortality, with 74 attributable deaths. Of these there were 27 septic abortions, which might have been helped by chemotherapy. Either chemotherapy was not considered or it was considered too late to be of any appreciable value. It is too much to hope that chemotherapy as we know it today can be of any curative value in peritonitis.

It is gratifying that the number of cases of pernicious vomiting has fallen, no cases having been reported. This means better earlier diagnosis and treatment, hence better obstetrics.

It is lamentable that cardiac disease has claimed 16 lives. These patients should never have been allowed to become pregnant; and if pregnant, they should have been aborted. The same may be said of the single patient who died of chronic nephritis.

Toxemias, with and without eclampsia, still take much too large a toll. Until obstetrics is more intelligently practiced, this number cannot be decreased. There will always be a few ignorant patients who do not present themselves for care until the disease is beyond help. Such deaths are not the fault of the medical profession.

Anesthetic deaths should be prevented; there were 4 in 1939. The 3 transfusion deaths are also

evidence of imperfect study and should be prevented.

Although the 1938 death rate from cesarean section per se is only 2.7, a more intelligent decision as to whether the operation is or is not necessary would reduce the number of cesareans done and would consequently lower the mortality from this cause.

It has come to the attention of the committee that some hospitals in Massachusetts are not following the *International List of Causes of Death* in making up their yearly reports. This list is followed at the State House, and should be used by every hospital in order that their yearly reports, based on the same criteria, may furnish accurate statistics. According to the *International List of Causes of Death*, every pneumonia occurring in pregnancy is classified as a maternal death, as is every cardiac death occurring during pregnancy. If this list were followed in all hospitals, their mortality rates would be honestly comparable.

The officers of the section are again grateful for the co-operation of the physicians in Massachusetts, and ask for their further support until this study has been completed.

DEATHS

DAVIS—FRANK A. DAVIS, M.D., of Hampton, New Hampshire, formerly of Boston, died October 8. He was in his seventy-fifth year.

He attended the University of New Hampshire and received his degree from Boston University School of Medicine in 1898. For nineteen years he practiced medicine in Boston. He was surgeon in the X-ray Department of the Boston Dispensary in 1905; in 1913 he was appointed physician-in-charge.

Dr. Davis received an honorary Sc.D. degree from the University of New Hampshire in 1913. In 1917 he enlisted in the Medical Corps of the United States Army and was later associated with the Veterans' Bureau in Washington and New York City. At the time of his retirement in 1929, he was in charge of the bureau's physiotherapy department in the Bronx, New York City.

He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow and three nephews survive him

ENEBUSKE—CLAES J. ENEBUSKE, M.D., of Lund, Sweden, formerly of Cambridge, Massachusetts, died July 4. He was in his eighty-sixth year.

Dr. Enebuske received his degree from Harvard Medical School in 1896. He was a member of the Massachusetts Medical Society and the American Medical Association.

LEONARD—WILLIAM J. LEONARD, M.D., of Provincetown, died July 25. He was in his seventy-first year.

Dr. Leonard received his degree from the College of Physicians and Surgeons of Baltimore in 1896. He was formerly police-department surgeon and city physician of Springfield. At one time he was on the staffs of the Mercy

Hospital and the City of Springfield Infirmary, Springfield.

Dr. Leonard was a former member of the Massachusetts Medical Society and the American Medical Association.

SWAN—ROSCOE W. SWAN, M.D., of Worcester, died October 13. He was in his eighty-first year.

Born in Framingham, he attended Chauncy Hall School, Massachusetts State College and Boston University and received his degree from Harvard Medical School in 1882. Dr. Swan practiced for eight years in Worcester and then studied in Europe for fourteen years, returning to Worcester in 1904 to specialize in intestinal diseases.

He was a member of the Massachusetts Medical Society and the American Medical Association and was also medical director of the Massachusetts Protective Association.

His widow survives him.

MISCELLANY

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR AUGUST, 1940

DISEASES	AUGUST 1940	AUGUST 1939	FIVE YEAR AVERAGE*
Anterior poliomyelitis	9	15	130
Chicken pox	81	120	108
Diphtheria	12	13	16
Dog bite	1206	1153	1102
Dysentery, bacillary	15	12	11
German measles	20	14	42
Gonorrhea	366	432	493
Lobar pneumonia	93	77	117
Measles	507	281	201
Meningococcus meningitis	3	2	5
Mumps	157	83	151
Paratyphoid B fever	36	3	10
Scarlet fever	78	82	129
Syphilis	297	367	445
Tuberculosis, pulmonary	319	317	305
Tuberculosis, other forms	28	27	33
Typhoid fever	12	10	12
Undulant fever	1	0	4
Whooping cough	509	429	468

*Based on figures for preceding five years

RARE DISEASES

Anterior poliomyelitis was reported from: Braintree, 1; Chicopee, 1; Holyoke, 2; Lynnfield, 1; Millbury, 1; Stockbridge, 1; Worcester, 2; total, 9.

Anthrax was reported from: Lynn, 1; total, 1.

Diphtheria was reported from: Adams, 1; Boston, 1; Canton, 1; Chelsea, 1; Framingham, 4; Leverett, 1; Somerville, 2; Wrentham, 1; total, 12.

Dysentery, bacillary, was reported from: Chicopee, 1; Danvers, 3; Lawrence, 1; Lowell, 4; Quincy, 1; Worcester, 5; total, 15.

Infectious encephalitis was reported from: Holyoke, 1; total, 1.

Meningococcus meningitis was reported from: Cambridge, 1; Hull, 1; Millbury, 1; total, 3.

Paratyphoid B fever was reported from: Beverly, 1; Cambridge, 1; Fall River, 1; Haverhill, 1; Lowell, 1; Lynn, 1; Somerville, 1; Tewksbury, 29; total, 36.

Pellagra was reported from: Boston, 1; total, 1.

Pfeiffer bacillary meningitis was reported from: Northampton, 1; total, 1.

Septic sore throat was reported from: Boston, 1; Fall River, 1; Saugus, 1; total, 3.

Tetanus was reported from: Fall River, 1; Somerville, 1; Worcester, 1; total, 3.

Trachoma was reported from: Boston, 1; total, 1.

Trichinosis was reported from Boston, 3, Haverhill, 1, total, 4

Typhoid fever was reported from Boston, 3, Holden, 1, Medford, 1, Quincy, 6, Springfield, 1, total, 12

Undulant fever was reported from Plymouth, 1 total, 1

Anterior poliomyelitis continued to show unusually low incidence

Measles, mumps, pulmonary tuberculosis and whooping cough were reported above the five year averages

Scarlet fever was reported at a record low figure both for this and any other month ever recorded

Diphtheria, lobar pneumonia, tuberculosis (other forms), German measles and chicken pox were reported below the five year averages

Meningococcus meningitis and undulant fever showed low incidence

Typhoid fever was reported at a figure equal to that of the five year average

Dog bite was reported at a record high figure
Animal rabies showed low incidence An active focus was noted in Hanover

NOTICES

ANNOUNCEMENTS

JACK GURWITZ, M.D., announces the opening of an office at 434 North Main Street, Randolph

AARON KAUFMAN, M.D., announces the removal of his office from 395 Commonwealth Avenue to 483 Beacon Street, Boston

JOSEPH SALAYER, M.D., announces the opening of an office at 111 West Main Street, Waterbury, Connecticut

PETER BENT BRIGHAM HOSPITAL

A joint medical and surgical clinic at the Peter Bent Brigham Hospital will be held on Wednesday, October 23, from 2 to 4 p.m. Drs E C Cutler and Soma Weiss will speak, their subject being "Abdominal Pain. A clinicopathological conference, conducted by Dr Elliott C Cutler, will take place from 4 to 5 p.m.

Physicians and students are cordially invited to attend

CARNEY HOSPITAL

The monthly clinical meeting and luncheon of the Carney Hospital will be held in Carney Hospital Auditorium on Monday, October 21, at 11 30 a.m.

PROGRAM

Business

Case Report

Clinicopathological Conference A case of acute pulmonary tuberculosis or of miliary tuberculosis Drs John L. Doherty, Edward J. Leonard and Francis J. Wenzler

Physicians and medical students are invited to attend

TRUDEAU SOCIETY OF BOSTON

There will be a meeting of the Trudeau Society of Boston in the auditorium of the Beth Israel Hospital on Thursday evening, October 24, at 8 00 Dr Richard H. Overholt will speak, his subject being "The Management of Pulmonary Abscess." The discussion will be opened by Drs Theodore L. Badger and Henry L. Cabott

BOSTON LYING IN HOSPITAL

A meeting of the medical alumni of the Boston Lying in Hospital will be held at the hospital on October 24. This has been designated as Walter Channing Day, in commemoration of one of the original founders of the hospital and the first professor of midwifery and medical jurisprudence at Harvard Medical School

The scientific portion of the program will be held in the amphitheater of Building D, Harvard Medical School, from 11 30 a.m. to 12 30 p.m. and from 2 00 to 4 00 p.m.

HARVARD MEDICAL SOCIETY

The next meeting of the Harvard Medical Society will be held on Tuesday, October 22, in the amphitheater of the Peter Bent Brigham Hospital at 8 15 p.m.

PROGRAM

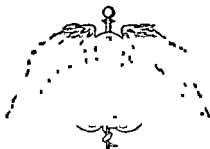
Presentation of Cases

Endocrine Control of the Reproductive Cycle

Pituitary Ovarian Interrelationships of the Estrous Cycle Dr F H Hisaw

The Regulation of Corpus Luteum Function Dr E B Astwood

BOSTON DOCTORS' SYMPHONY ORCHESTRA



The Boston Doctors' Symphony Orchestra will rehearse under Alexander Thiede, former concert master with the Cleveland Symphony Orchestra, every Thursday at 8 30 p.m. Those interested in becoming members should com-

municate with Dr Julius Loman, Pelham Hall Hotel, Brookline (BEA 2430)

MASSACHUSETTS GENERAL HOSPITAL

A meeting of the Hospital Research Council will be held in the Ether Dome of the Massachusetts General Hospital on Tuesday, October 29, at 5 00 p.m.

PROGRAM

Clinical Aspects and Renal Function Dr John H. Talbot

Constituents of Blood and Respiratory Functions Drs D Bruce Dill and William H. Forbes

Therapeutic Considerations in Schizophrenia Dr Kenneth J. Tiltonson

TAUNTON STATE HOSPITAL

The Taunton State Hospital, Taunton, Massachusetts, announces the extension of its clinic facilities. Beginning the week of October 13 child guidance clinics, where children with their special problems may be studied, and later treated, will be held in the City Hall Annex, Fall River, each Tuesday, and in the Olympia Building, New Bedford, each Wednesday, from 1 00 to 4 00 p.m. by appointment. Mental health clinics for adults will be held in Fall River each Tuesday and in New Bedford each Wednesday, between 9 00 and 11 30 a.m. Those who desire consultation with a psychiatrist will be welcomed, but appointment must be made, as in the past, through a social agency or a physician.

NORFOLK DISTRICT MEDICAL SOCIETY

A stated meeting of the Norfolk District Medical Society will be held at the Hotel Puritan, Boston, on Tuesday evening, October 29, at 8:00 (Tel. KEN 1480).

PROGRAM

Business.

Medical Preparedness. Drs. Thomas R. Goethals, Frederick J. Bailey and Donald E. Currier.

Discussion.

Collation.

MASSACHUSETTS SOCIETY
FOR MENTAL HYGIENE

The Massachusetts Society for Mental Hygiene announces that the Northeastern Conference on Mental Health in the Community will be held in Salem at the Hotel Hawthorne and the Lydia E. Pinkham Memorial on Friday, November 15. This will be an all-day conference, with morning, afternoon and evening sessions.

The speaker of the evening will be Dr. Ira S. Wile, formerly commissioner of education, New York City, who will discuss the central theme of the conference—"The Mental Health of the Community."

There will be a special luncheon for physicians at the Hotel Hawthorne at 12:30 p.m. Dr. Harry C. Solomon, associate professor of psychiatry, Harvard Medical School, will speak, his subject being "The Diagnosis and Treatment of Mental Disorders." All physicians, especially those in the northeastern part of the State, are welcome.

This conference has been endorsed and is being sponsored by the Essex South District Medical Society.

SOCIETY FOR RESEARCH
IN CHILD DEVELOPMENT

The Society for Research in Child Development is holding its fourth biennial meeting at the Harvard Medical School on November 8 and 9. This is a national organization of scientific workers who are actively studying some phase of the development of children. The membership of this society represents a wide variety of scientific disciplines, and this breadth of interest of the membership is reflected in the program. The latter contains reports of interest to the pediatrician, physiologist, nutritionist, psychologist, dentist and persons in other special fields. The primary purpose of the meetings of this society, however, is to bring together persons with widely divergent experiences and interests, to familiarize those in each field with the advances which have been made in the other fields, and to apply these collective advances to the better understanding of the total development of children.

A fee is charged for registration, which assures accommodation at all the meetings, but students and members of the interested professions will be admitted to individual sessions, without registration, so far as space permits at the time scheduled. The topics and times of the various sessions are as follows:

FRIDAY MORNING, NOVEMBER 8. Harvard Medical School, Amphitheater, Building E.

9:30-11:00 Panel discussion of technical problems involved in longitudinal studies of physical growth.

11:10-12:40 Panel discussion of technical problems involved in longitudinal studies in the psychological area.

11:15-12:45 Dental and nutritional studies being conducted at the Forsyth Dental Infirmary. This session will be held at the Forsyth Dental Infirmary.

FRIDAY AFTERNOON, NOVEMBER 8. Harvard Medical School Amphitheater, Building G.

2:00-5:00 Symposium on neurological and behavioral characteristics of the newborn.

SATURDAY MORNING, NOVEMBER 9. Harvard Medical School Amphitheater, Building B.

9:00-12:00 Symposium on adolescent development.

SATURDAY AFTERNOON, NOVEMBER 9. Children's Hospital Amphitheater.

2:00-3:00 Reports of studies of child development from the Center for Research in Child Health and Development, Harvard School of Public Health.

3:30-5:00 Studies of development following injury to the central nervous system in early life.

Those interested in obtaining further details as to the topics covered and the participants in the various sessions listed may obtain the same by communicating with the Department of Child Hygiene, Harvard School of Public Health.

AMERICAN CONFERENCE
ON INDUSTRIAL HEALTH

Industrial physicians and manufacturers from all over the country will attend the American Conference on Industrial Health to be held Thursday, November 14, at the Towers Club in Chicago. The conference will be sponsored by the American Association of Industrial Physicians and Surgeons, a 25-year-old organization.

This first meeting of the American Conference on Industrial Health has for its purpose the correlation of viewpoints of all persons who are interested in promoting industrial health. These include employers, physicians, industrial hygienists, labor organizations, psychiatrists, insurance companies, public relations men, safety experts and the legal profession.

Dr. Clarence O. Sappington, of Chicago, co-chairman of the committee with Dr. Edward C. Holmblad, stated: "We have invited the manufacturer and other persons to attend and participate in the convention so that we may prove the practical value and application of industrial health work, and so that they may realize how much time and money may be saved yearly by such measures."

Among the prominent speakers who will talk at the convention sessions are: Dr. Morris Fishbein, editor of the *Journal of the American Medical Association*; Mr. B. C. Heacock, president of the Caterpillar Tractor Company; Dr. Volney S. Cheney, medical director of Armour and Company; and Mr. J. M. Conway, representing the National Association of Manufacturers, New York City.

The conference, which is scheduled to begin at 9:30 a.m., will conclude with a dinner session, at which Dr. Fishbein and Mr. Conway will speak.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING
SUNDAY, OCTOBER 20

SUNDAY, OCTOBER 20

*7 p.m. Medical Horizons. Dr. Nathan B. Van Etten. St. Paul's Cathedral, Boston.

MONDAY, OCTOBER 21

*11:30 a.m. Carney Hospital, monthly clinical meeting and luncheon.
12:15-1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

TUESDAY, OCTOBER 22

*9-10 a.m. Simple X-Ray of the Skull as an Aid to Neurological Diagnosis. Dr. Kurt Goldstein. Joseph H. Pratt Diagnostic Hospital.

- 12 15-1 15 p.m. Clinico-orthogenological conference Peter Bent Brigham Hospital Amphitheater
 8 15 p.m. Harvard Medical Society Amphitheater Peter Bent Brigham Hospital Page 647
- WEDNESDAY OCTOBER 23**
 *9-10 a.m. Hospital case presentation Dr S J Thannhauser Joseph H Pratt Diagnostic Hospital
 *12 m Clinico-pathological conference Children's Hospital
 *2-4 p.m. Abdominal Pain Drs E C Cutler and Soma Weiss Joint medical and surgical clinic Peter Bent Brigham Hospital
- THURSDAY OCTOBER 24**
 *9-10 a.m. Hemorrhagic Diathesis Dr Eugene Lozner Joseph H Pratt Diagnostic Hospital
 11 30 a.m.-12 30 p.m. and 2-4 p.m. Walter Channing Day Boston Lying in Hospital
 8 p.m. The Management of Pulmonary Abscess Dr Richard H Overholt Trudeau Society of Boston Auditorium Beth Israel Hospital
- FRIDAY OCTOBER 25**
 *9-10 a.m. Clinicopathological conference Dr Fuller Albright and Dr H E MacMahon Joseph H Pratt Diagnostic Hospital
 8 15 p.m. Massachusetts Memorial Hospitals staff meeting
- WEDNESDAY OCTOBER 26**
 *9-10 a.m. Hospital case presentation Dr S J Thannhauser Joseph H Pratt Diagnostic Hospital
 *Open to the medical profession

- OCTOBER 14-25—1940 Graduate Fortnight of the New York Academy of Medicine Page 305 issue of August 22
 OCTOBER 21—American Board of Internal Medicine Page 369 issue of February 29
 OCTOBER 29—Massachusetts General Hospital Hospital Research Council age 647
 NOVEMBER 8-9—Society for Research in Child Development Page 648
 NOVEMBER 13, 14—New England Postgraduate Assembly Cambridge Massachusetts
 NOVEMBER 14—Pennsylvania Association of Physicians Page 263 issue of August 15
 NOVEMBER 14—American Conference on Industrial Health Page 648
 NOVEMBER 15—Massachusetts Society for Mental Hygiene Page 648
 DECEMBER 27-29—National Convention of the Association of Medical Women Boston
 JANUARY 4 1941—American Board of Obstetrics and Gynecology Page 604 issue of June 20
 MARCH 8—American Board of Ophthalmology Page 201 issue of August 1
 APRIL 21-25—American College of Physicians Page 1065 issue of May 20
 MAY 21 22—Massachusetts Medical Society Boston
 JUNE 2-6—American Medical Association Cleveland Ohio

DISTRICT MEDICAL SOCIETIES

- WORFOLK**
 OCTOBER 29—Page 648
- SUFFOLK**
 OCTOBER 30—Page 604 issue of October 10
 NOVEMBER 7—Censors meeting Page 305 issue of August 22
 JANUARY 29—Page 604 issue of October 10
 APRIL 30—Page 604 issue of October 10
- WORCESTER**
 NOVEMBER 13—Grafton State Hospital Grafton
 DECEMBER 11—St Vincent Hospital Worcester
 JANUARY 8 1941—Worcester City Hospital Worcester
 FEBRUARY 12—Worcester State Hospital Worcester
 MARCH 12—Memorial Hospital Worcester
 APRIL 9—Hahnemann Hospital Worcester
 Supper will be served at 6 30 p.m. followed by a business meeting and a social program

BOOK REVIEWS

Principles of Orthopedic Surgery By James Warren Weaver, M.D. Third edition 8", cloth, 418 pp., with 220 illustrations New York: Macmillan Company, 1940 \$3.25

The third edition of this textbook by a well known representative of the Boston School of Orthopaedic Sur-

gery' shows an admirable attempt to bring the book up to date. It is written in a clear, concise manner. The suggestions for treatment and the conclusions are practical. The care of the patient, particularly the nursing care, is treated adequately. The content of any textbook is dependent largely on the experience of the author, thus, in this treatise, juvenile diseases and deformities are discussed at length, but the orthopedic disabilities of adults are only briefly mentioned. Tuberculosis of the bones and joints is probably given more attention than the disease merits at the present time. The excellent chapter on the use of apparatus would probably be improved by a few line drawings of the braces that are discussed. For doctors and medical students the work can be recommended as a supplementary textbook. For the teaching of nurses, physiotherapists and others who aid physicians in the care of orthopedic disabilities it can be recommended unreservedly.

Carbohydrate Metabolism: Four papers presented in a symposium held at the meeting of the American Physiological Society at Toronto, Canada, April 29, 1939 Reprinted from *Endocrinology*, 26 285-351, 1940. By various authors 4", paper, 67 pp., with 6 charts and 14 tables Menasha, Wisconsin: George Banta Publishing Company, 1940 \$1.00

Four papers, presented in a symposium on carbohydrate metabolism at the Toronto meeting of the American Physiological Society in April, 1939, have been reprinted in pamphlet form from *Endocrinology*. It would be difficult to find a more outstanding group of workers in this field than are here represented. The chairman of the symposium was Professor C H Best, and those participating included C F Cori, Samuel Soskin, C N H Long, and F G Young, of London, England.

In the first paper Cori discusses glycogen breakdown and synthesis in animal tissues. No one is better qualified to speak of glycogen than is this investigator, who has participated in much of the best recent research work concerning it. He emphasizes the fundamental importance of the enzymes which are concerned in the degradation and synthesis of glycogen. It is on them that changes in liver and muscle glycogen depend, and through them that insulin, epinephrine, and other hormones act.

Soskin's contribution is entitled "The Liver and Carbohydrate Metabolism." He presents some of the newer evidence which invalidates the orthodox interpretations of the D/N ratio, the RQ, and the production of ketone bodies. He reviews some of the recent work showing that glycogen is formed from fatty acids in the liver and that the completely diabetic organism does utilize sugar to a certain extent. He shows that the regulation of the blood sugar level lies primarily in the liver and its glycogen mechanism, not in the pancreas and insulin production.

The adrenal cortex and carbohydrate metabolism are dealt with by Long, Katzin and Fry, of the Department of Physiological Chemistry, Yale University. In carefully controlled experiments with rats and mice they show that the adrenocortical hormone has a direct, positive action on carbohydrate and protein metabolism, causing a marked rise in liver glycogen and blood sugar at the expense of increased protein catabolism, in both normal and adrenalectomized animals. The hormone also has a diabetogenic effect in hypophysectomized, partially depancreatized rats, which is synergistic with that of anterior pituitary extract.

Young, in a brief paper on the pituitary gland and carbohydrate metabolism discusses a number of different

effects of anterior pituitary extracts which may be concerned in the production of diabetes in normal animals by the injection of such extracts. He distinguishes an insulin-insensitivity effect, which may occur without any rise in the blood-sugar level; a ketogenic effect, which may result through diminished catabolism of carbohydrate and protein; a diabetogenic effect, including glycosuria in normal animals and possibly due to a diminished rate of insulin secretion by the pancreatic islets; and a pancreotropic effect, involving hyperplasia of islet tissue. There is evidence that the diabetogenic factor may be related to, or even contained in, the growth hormone.

This symposium affords an excellent review of significant recent work in carbohydrate metabolism.

Modern Medical Therapy in General Practice. Vol. 1, 2 and 3. Edited by David Preswick Barr, A.B., M.D., LL.D., Busch Professor of Medicine, Washington University; and physician-in-chief, Barnes Hospital, St. Louis. 4°, cloth: Vol. 1, 1230 pp., with 111 tables, 65 figures and 3 plates; Vol. 2, 1282 pp., with 42 tables, 20 figures and 5 charts; Vol. 3, 1215 pp., with 19 tables and 43 figures. Baltimore: Williams & Wilkins Company, 1940. \$35.00.

In three enormous volumes, weighing over 16 pounds, the whole subject of modern medical therapy is considered under the direction of Dr. David P. Barr, physician-in-chief to the Barnes Hospital, St. Louis, and professor of medicine, Washington University.

The vast undertaking is the result of a co-operative endeavor by many of the outstanding physicians of America. Each subject is considered in detail by a specialist in the field, and all the papers are brought together under careful editorship. The work is divided into sections on general diseases, infectious diseases, diseases of the nervous system, diseases of the gastrointestinal tract and diseases of the other organs and systems. The volumes, therefore, cover the whole field of medicine, including specialized parts, such as the skin, the ear and the eye. Surgical treatment is occasionally mentioned, but the entire work is devoted almost exclusively to medical treatment.

Like any work of this type, there is marked variation in the value of the chapters. Some are carefully written by men obviously well qualified; others are of less value. One of the best sections of the book is that contributed by Dr. Barr on the use of drugs in relation to general therapy. There are excellent articles, however, by other men, details of which cannot be given in a brief review. In general, these volumes have set a high standard, and the work can be recommended. In many chapters, there are references to the literature, although there seems to be no uniformity in regard to this important aspect of medical literature. A few mistakes, moreover, have crept into the bibliographies.

It should be pointed out that all material in a book of this type cannot be accepted as the best form of treatment for any individual patient. For example, physicians specializing in such subjects as electrotherapy, physiotherapy and occupational therapy are likely to overemphasize the importance of their particular field of endeavor. This is certainly true in this book, and unfortunately the editor has not seen fit to curtail a certain amount of overenthusiasm expressed in some of the articles.

One unusual feature of the book is the relative lightness of the enormous volumes. They are, however, too large, and the work would have been much more useful had it been divided into six or eight volumes rather than three. There are a few illustrations, which do not add much to the value of the text.

International Medical Annual: A year book of treatment and practitioner's index. Edited by H. Letheby Tidy, M.A., M.D. (Oxon.), F.R.C.P., and A. Rendle Short, M.D., B.S., B.Sc., F.R.C.S. 8°, cloth, 545 pp., with 65 plates. Baltimore: Williams & Wilkins Company, 1940. \$6.00.

This sound digest of medical thought continues, after fifty-eight years of existence, to be the leading publication of its kind in the field. Written by British physicians of outstanding merit, the articles, carefully documented and illustrated, are brief essays on the latest developments in medicine. In arrangement and size the volume does not differ from its predecessors. It is difficult to think of any physician, whatever his particular field of interest, who would not profit by a thoughtful perusal of this volume.

L'Examen du Malade. By P. Delmas, G. Giraud, E. Jeanbrau, E. Leenhardt, J. Margarot, P. Pages, V. Riche L. Rimbaud, J. Terracol and H. Villard, professors of the Faculty of Medicine of Montpellier. 12°, paper, 365 pp. Paris: Masson et Cie, 1939. 45 Fr. fr.

The second edition of this book shows considerable improvement over the first issue by introducing diagnosis in the field of psychiatry and endocrinology. On the whole it is an excellent summary of most of the common present day diagnostic methods. Short and to the point, it can be considered a review book of merit.

Studies in the Development of Young Children. By Nancy Bayley. 8°, paper, 45 pp., Berkeley University of California Press, 1940. 35 cents.

This pamphlet embraces studies of 61 Berkeley children: 30 girls and 31 boys, during the first decade of life. Growth and development in body, mind and personality are considered, plus the influence of disease and other factors in the environment. The discussions are, however, of the briefest, and as they stand, give rise to no new conclusions. They need amplification or extension, or both to be of value.

Mammalian Genetics. By William E. Castle, Ph.D., Sc.D. 8°, cloth, 169 pp., with 131 illustrations and 8 tables. Cambridge: Harvard University Press, 1940. \$2.00.

No author could be better qualified than Dr. Castle to write an introduction to mammalian genetics. This volume should make a strong appeal to students in colleges, particularly when it is used in conjunction with the laboratory guide prepared by the same author. The illustrations are clear cut. There are references at the end of each of the nineteen chapters. A discussion of the heredity of man is not included in this book because heredity has to be investigated by methods other than those of experiment.

Dr. Castle shows that the general features of organization are probably dependent on the general features of organization of the living substance in each group and that the details of organization are inherited in accordance with Mendel's law. He points out that the uniting gametes although not different morphologically may vary physiologically. In the chapter on sex determination consideration is given to the operation of three different agencies: chromosomal, environmental and endocrine. It is significant to note that the author thinks it illogical to ascribe action either to nuclear activity alone or to plasmatic activity alone; the two acting together should be considered. This book will no doubt be on the shelves in every biological library and laboratory.

The New England Journal of Medicine

Copyright, 1940, by the Massachusetts Medical Society

VOLUME 223

OCTOBER 24, 1940

NUMBER 17

SYMPOSIUM ON INFECTIONS OF THE RESPIRATORY TRACT

OBSERVATIONS ON THE EPIDEMIOLOGY OF THE COMMON COLD*

WILSON G. SMILLIE, M.D.†

NEW YORK CITY

THE common cold is a paradox. It is so common—or rather so prevalent—that no one is interested in it. We are all familiar with the statistics which indicate that colds cause more loss of time from business than do all other illnesses combined. This is true. They do cause loss of time from work, no doubt, but no serious loss of time, I suspect, from more pleasurable pursuits.

The disease is so exasperating: it never kills and seldom causes serious illness, but it refuses to submit to any known therapeutic or preventive measures. It is not a disease at all. It is a group of diseases, masking themselves under a homogeneous assembly of similar clinical symptoms, with a pretense of being a single clinical entity, but in reality being of widely diversified etiology.

We are accustomed to the statement that a cold is an acute inflammation of the upper respiratory tract. But almost all the communicable diseases of childhood are initiated by symptoms of an acute infection of the upper respiratory tract. Measles, scarlet fever, whooping cough, tonsillitis, diphtheria—all in their initial stages resemble an upper-respiratory infection.

The sinus infections are often confused with colds. One frequently hears the statement, "I caught cold in the fall, and it lasted off and on all winter." The patient really has had recrudescences of chronic sinusitis from time to time. The common opinion that a cold is due to exposure results from the fact that a person with sinusitis may have the infection under control, but following exposure to cold, chilling of the body sur-

face, fatigue or other factors the sinus infection reasserts itself, and the patient complains of a "fresh" cold.

Persons with unknown susceptibility to certain proteins often develop symptoms of the upper respiratory tract, and complain about the prevalence of colds. Mechanical irritations of all sorts, which affect the mucous membranes of the nose and throat, produce what to the patient are symptoms of an early infection; but by appropriate home remedies he manages to "break up" his cold in twenty-four hours. All these various conditions are grouped in one diagnosis—a common cold.

One disease entity may be singled out of this group of ills, namely, the acute self-limited epidemic infection of the upper respiratory tract. This infection is due to a filterable virus. It is transmitted readily, and by fairly direct contact, from person to person. Wells¹ has shown that the zone of transmission is not simply the distance of spread of the direct spray of the sneeze or cough of the infected person, but the infecting agent may actually spread in a radiating zone for a considerable distance, particularly within the confines of a building, such as a schoolroom or a theater.

The incubation period is short—twenty-four to thirty-six hours. The infected individual communicates his infection to others for a short period only—during the early stages. Three or four days after the beginning of symptoms he is non-infectious, although he may continue with sore throat and cough for a long time. The most infectious period is the initial day, and a patient may even infect others from four to six hours

*This and the following three papers were presented as a symposium at the annual meeting of the Massachusetts Medical Society, Boston, May 21, 1940.

†Professor of public health and preventive medicine, Cornell University Medical College, New York City

before he is aware that he is coming down with a cold.

The carrier state, common in so many infections, is believed to be quite rare. We do not know with certainty how frequently it occurs, but all evidence indicates that carriers of the virus of colds or of influenza are rarely if ever encountered.

The degree of contagiousness is high. Practically all susceptible persons who are exposed to immediate contact with an infected person develop the disease. The immunity that is produced from an attack of this disease is specific, but may be of relatively short duration. Individual resistance varies considerably, tending to increase with age. It is quite certain that attacks are much less frequent in the older age groups. There is a great variation in susceptibility among the members of a single family or in a closed community, as a boarding school or an orphanage.

Francis² has shown, in his studies of influenza, that individual immunity may be due to protective bodies, which are found in the nasal secretions. These secretions are not destructive to bacteria, but may have a high power of neutralization of the influenza virus. There is a great deal of variation in the destructive power of these secretions. The question arises as to whether the potent factor is a nonspecific enzyme, or whether the protective bodies in these secretions are specific and bear the same relative immune power as does the blood serum or other body tissues.

The only experimental animal that has been employed successfully in the study of colds is the chimpanzee. Thus, all experimentation becomes complex and very expensive. The influenza virus, on the other hand, is transmissible to ferrets and young white mice.

I have included influenza in my discussion of the common cold. The reason is that, clinically, the acute epidemic respiratory infections themselves are not a single entity, but a group of diseases which show wide variation in symptomatology and in degree of severity. Even in an epidemic of known single etiology, all gradations of clinical symptoms may be encountered. For example, I³ have studied the epidemiology of a severe infection of the upper respiratory tract at Northwest River, Labrador. The colony of 167 persons was cut off from all communication with the outside world by ice and snow. A dog-team driver went to Rigolette, eighty miles away, for the Christmas mail. There he found an epidemic of severe respiratory infection raging. Without delay he loaded his sled and returned home. Twenty-four hours later, while still half a day's journey from home,

he became very ill but strapped himself on the sled and the dogs took him home. This infectious agent, brought in by a single individual, produced in this small village an epidemic of disease. The striking feature of the epidemic was that all variations and gradations in symptoms occurred in the patients—from a simple mild ambulatory cold to a severe debilitating influenza with post-influenzal pneumonia, and even death.

Horsfall, Hahn, and Rickard,⁴ in a recent study of four epidemics of mild influenza, conclude that the certain diagnosis of epidemic influenza cannot be made on either clinical or epidemiologic grounds. Neither can it be made from serologic tests. Infected individuals developed specific antibodies, it is true, but some exposed persons remain symptom-free, yet develop specific antibodies equal to those shown by the frank cases.

Martin and Fairbrother⁵ recently described an epidemic of apparent influenza that occurred in 1939 in England. It was a uniform disease occurring in a closed community. Clinically it resembled influenza, except for lack of severity and limited dispersion. Ferrets were infected on first passage, but the virus died out on second passage. It was too mild a disease to be called influenza, too severe to be called a common cold.

Magill and Francis,⁶ in a study of twenty-four strains of influenza virus, have shown that there is a marked variation in antigenic characteristics of the different strains. Some strains from a single epidemic closely resemble one another, but strains from different epidemics show great variation. These authors suggest that the structure of the virus of epidemic influenza is a mosaic of antigens, and that each strain does not contain all, or even a major part, of the antigenic components of other strains.

Do these findings not suggest that all the acute epidemic infections of the upper respiratory tract, from the mildest to the severe pandemic infections, are due to a closely related group of infectious agents which have wide gradations in virulence, and which produce a chain of symptoms varying in degree and kind from the very mild to the very severe—from an ambulatory cold to a fatal influenza? In any given outbreak the virulence will be fairly constant, but even when the virus is known to be exactly the same, as, for example, in the Labrador epidemic and also in the epidemic described by Martin and Fairbrother, different individuals within a single community or even a single family will vary widely in their reactions to the infection.

There does not seem to be much hope of developing an effective specific vaccine against the

milder common colds. It seems probable, on the other hand, that a method may be devised whereby an individual may be immunized against the virulent specific prevailing epidemic influenza virus—if it can be isolated, sent ahead of the epidemic and administered just before the arrival of the infection in the community. But immunization against seasonal colds is another matter. One can hardly expect the physician to do more than Nature herself in producing an immunity to this type of infection. Nature does not produce more than temporary immunity through the actual attack of a cold. Thus, we cannot expect that specific preventive measures could produce more lasting immunity than does an actual attack of the disease itself.

We must admit that there is no known way of preventing epidemics of colds in the active life of a modern civilization. In so far as this infection itself is concerned, it is of little importance whether we do or do not prevent the ordinary mild cold. Unfortunately, however, the acute cold is frequently followed by serious consequences. The important features of the cold are its sequelae. The cold itself is a self-limited disease of four or five days' duration. In itself, it does little or no harm. But the virus may cause an injury to the mucous membranes of such degree as to permit secondary invaders to produce serious trouble. Apparently the consequences are dependent on the type of secondary invader that prevails in the nasopharynx at the moment. The commonest offender is the pneumococcus. The more virulent the type, the greater may be the degree of invasion and injury.

Recently I have taken serial nasopharyngeal cultures in an orphans' home. Pneumococcus Type 14 appeared and spread through the nursery until practically every child was a carrier of the strain. There were no ill effects, although Type 14 is notoriously a frequent cause of pneumonia in children. An epidemic of colds then invaded the nursery. Promptly the Type 14 pneumococcus increased in prevalence in the throats of the children. Furthermore, the inflammation extended from the posterior nasopharynx to the middle ear in several of the group, and two children developed pneumonia. In every case the Type 14 pneumococcus was isolated from the discharges of the ears and from the sputum of the children with pneumonia.

The prevailing organism that may be quiescent and then suddenly cause serious trouble, following an acute cold, is not always a pneumococcus. For example, a patient had a troublesome acute sinus

infection. A beta hemolytic streptococcus was isolated in almost pure culture from the discharges. A month's vacation in a warm, dry climate resulted in quiescence, although cultures showed that the same organism was still present in the sinus discharges in small numbers. On the day of return from the tropics, the patient was exposed to a person who was in the first stages of a cold. The hour and moment of first exposure were known. An acute cold developed promptly, and was followed in three days by a recrudescence of the sinus infection. Culture of the discharges showed enormous numbers of beta hemolytic streptococci. The individual from whom the cold was acquired did not harbor a beta hemolytic streptococcus, but was a carrier of Type 8 pneumococcus. He also developed a sinusitis, but the invading organism in his case was Type 8 pneumococcus.

If the secondary invaders are the important factors in production of the severe sequelae of acute respiratory infections, can nothing be done to increase the immunity of an individual to these organisms and prevent the severity of the effects?

Cold vaccines have not been wholly successful in the past for two reasons. In the first place, they do not build immunity against the invasion of the initial virus; in the second place, they do not always increase the resistance of the individual to the specific secondary organism to which he may be exposed.

Theoretically, at least, it would seem to be quite possible to prepare a cold vaccine from the organisms which are most prevalent in the nasopharynxes of the community, and to which the individual is most likely to be exposed. Immunization with this vaccine should give some degree of protection against the prevailing and most troublesome factors which produce the more serious consequences of the common cold.

SUMMARY

The common cold is an epidemic virus infection of the upper respiratory tract. It is frequently confused with other clinical conditions. It is so closely related to influenza that no clear-cut clinical differentiation is possible at the present time. The disease is self-limited, is of four or five days' duration and, of itself, is of little consequence.

The importance of the infection depends on the fact that the virus prepares the mucous membranes of the upper respiratory tract for invasion with a wide variety of organisms with which we are quite familiar, and concerning which some preventive measures may be taken.

REFERENCES

1. Wells, W. F.; Stokes, J., Jr.; Wells, M. W., and Wilder, T. S.: Experiments in the environmental control of epidemic respiratory infection. *Tr. & Stud., Coll. Physicians, Philadelphia* 7:342-344, 1940.
2. Francis, T., Jr., and Magill, T. P.: Immunological studies with the virus of influenza. *J. Exper. Med.* 62:505-516, 1935.
3. Smilie, W. G.: An epidemic of influenza in an isolated community—Northwest River, Labrador. *Am. J. Hyg.* 11:392-398, 1930.
4. Horsfall, F. L., Jr.; Hahn, R. G., and Rickard, E. R.: Four recent influenza epidemics: an experimental study. *J. Clin. Investigation* 19:379-392, 1940.
5. Martin, A. E., and Fairbrother, R. W.: An epidemic of apparent influenza. *Lancet* 2:1313-1315, 1939.
6. Magill, T. P., and Francis, T., Jr.: Antigenic differences in strains of epidemic influenza virus: cross-neutralization tests in mice. *Brit. J. Exper. Path.* 19:273-284, 1938.

THE RELATION OF SINUSITIS TO CHRONIC NONTUBERCULOUS CHEST INFECTION*

ROBERT L. GOODALE, M.D.†

BOSTON

THE purpose of this paper is to present the results of a study of the relation of sinusitis to bronchiectasis. During the last four years I have examined 150 cases of bronchiectasis at the Pulmonary Clinic of the Massachusetts General Hospital to determine the incidence of sinus infection, and to throw light, if possible, on the relation of sinusitis to the infection in the chest.

In a previous paper I¹ set forth the statistical features of this association of sinusitis with bronchiectasis. They are as follows:

(1) The patients were for the most part adults or adolescents at the time of examination.

(2) One third of the patients developed bronchiectasis in the first decade of life, and two thirds developed it before the age of twenty. The remaining cases were scattered throughout the third, fourth, fifth and sixth decades.

(3) The two commonest diseases which preceded the bronchiectasis were upper-respiratory infection (43 per cent) and pneumonia (29 per cent). The remainder were such conditions as influenza, whooping cough, asthma, tonsil and adenoid operations, and the presence of foreign bodies.

(4) Patients who developed bronchiectasis before the age of ten had had pneumonia more frequently than any of the other diseases. Most cases which developed after the age of ten gave a history of a previous upper-respiratory infection.

(5) Most of the male patients had had a preceding upper-respiratory infection more frequently at onset, while most of the female patients attributed their bronchiectasis to pneumonia, influenza or whooping cough.

(6) There was a very high incidence of sinusitis. Even among those who claimed not to have had an upper-respiratory disease at or preceding the onset, x-ray studies demonstrated an incidence of chronic sinusitis of 55 per cent; for the group as a whole the incidence was 62 per cent. The sinusitis varied in severity from an extremely slight thickening of the lining of the sinus involved, through all degrees up to a marked pansinusitis with chronically thickened mucous membrane, retained purulent secretion and, sometimes, reaction in the surrounding bone. In addition, 24 per cent of the others gave clinical evidence of recurrent acute sinusitis, so that the patients who suffered from more or less sinusitis totaled 86 per cent. The sinuses most frequently involved were the antrums and the ethmoids.

(7) Cases of bronchiectasis in which only one lobe was affected had a lower incidence of sinusitis than did those in which more than one were affected. Cases in which the left lower lobe alone was involved had an incidence of 45 per cent. For both left lobes the incidence was 60 per cent; for both lower lobes, 67 per cent; for the left lower and right middle lobes, 73 per cent; and for panbronchiectasis, 75 per cent. These facts are, of course, of great importance in evaluating the role of sinusitis in cases where thoracic surgery is considered.

In summary of the above points there seem to be several different diseases that occur at the onset of bronchiectasis. There is a very high incidence of sinusitis in these cases in later life. Even those cases that give an etiology of essentially pulmonary infection at the onset have a later sinusitis incidence of 55 per cent. Practically all show a marked susceptibility to respiratory infection. There may be factors in childhood differing from those existing in later life, and there may be certain predispositions in the sexes which make

*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 21, 1940.

†Instructor in laryngology, Harvard Medical School; associate surgeon, Massachusetts Eye and Ear Infirmary.

men more susceptible to one etiologic factor and women to another.

Because of the frequency with which sinusitis is found in cases of chronic cough, it has been thought by many observers that there is a direct relation, a mechanism, as it were, whereby the infection in the sinus causes that in the chest. This has been described as an absorption of toxins into the lymphatic system or blood stream, eventually affecting the lungs. There is also the question of direct inhalation into the lungs of septic postnasal discharge.

It is quite possible that at the time when a patient develops bronchiectasis there may be a severe head cold or a sinusitis in addition to a pulmonary infection, such as pneumonia. On the other hand, there are many patients with sinusitis who never develop any bronchial infection. In the latter the disease is purely local. But it is true that many patients with sinusitis suffer also from a cough and a great deal of postnasal discharge. The cough has been emphasized as an important cause of bronchial dilatation. It is also possible that in-

type one must be extremely conservative, unless one is faced with serious complications, such as intracranial infection, osteomyelitis or orbital abscess. In the chronic cases there is quite a different problem. In the very mild cases no operation may be needed, or if the patient is subject to repeated attacks of sinusitis and these infections are complicated by local conditions in the nose, such as a deviated septum, it may suffice to correct this obstruction. In children, the removal of tonsils and adenoids, the aspiration of nasal secretion and attention to the medical problems of hygiene have to be considered. It is in the more severe chronic infections in adults that radical operations may be necessary.

From the present series of 150 cases of bronchiectasis, 76 have been chosen to illustrate some of these points. These have been subdivided into four groups as follows: a control group of 21 cases in which the sinuses were negative but which received lobectomy; 14 cases of lobectomy in which the sinuses had not been operated on; 11 cases with both lobectomy and sinus surgery; and 30

TABLE 1. *End Results in 150 Cases of Bronchiectasis.*

TREATMENT	NO OF CASES	DEGREE OF IMPROVEMENT				
		SYMPTOM FREE	MARKED	MOD-ERATE	SLIGHT	NOVE
Lobectomy (sinuses negative)	21	8	8	5	0	0
Lobectomy (sinusitis—no surgery)	14	0	10	0	0	4
Lobectomy and sinus surgery	11	0	7	2	2	0
Sinus surgery	30	3	13	0	4	10
Totals	76	11	38	7	6	14

fect secretion may find its way into a bronchus and thereby cause a foreign-body obstruction with collapse of the lobe. There is still another situation which may occur. At the onset, the patient may have an infection of the entire respiratory tract. Because of the severity of the chest infection, the upper-respiratory features may be overlooked. The upper-respiratory infection, indeed, may soon clear up although the pulmonary damage persists. But as these patients suffer from more than the usual number of head colds, the opportunity for reinfection of the sinuses is very great and eventually a condition of chronic sinusitis may develop.

Each case presents its own problem in regard to treatment. After making a diagnosis of sinusitis, it is necessary to determine whether it is a major factor in the picture or whether it is of minor importance. This is naturally true of all cases of sinusitis, and the criteria hold true even in cases uncomplicated by bronchiectasis. There are all degrees of sinusitis. The proper treatment of an acute sinusitis, as is well known, is quite different from that of a chronic sinusitis. In the acute

cases in which the pulmonary disease was unsuitable for lobectomy or in which lobectomy, although indicated, had not yet been performed, and in which the sinuses were operated on (Table 1).

In the first group, where lobectomy was performed but the sinuses were negative, the results were the best. Out of 21 cases, 8 are now symptom-free, 8 have only a slight amount of sputum, and 5 have a moderate amount of sputum but have been improved. This group is also less subject to upper-respiratory infection.

In the second group, that of lobectomy and unoperated sinusitis, 10 of the 14 patients have been markedly improved in regard to the amount of sputum. Three of these 10 patients still have a moderate degree of sinusitis; although they are still subject to many head colds and to nasal discharge, their chests are negative. What sputum they have may well come postnasally from the sinuses. The remaining 4 patients have the same amount of sputum as before operation and a moderate to marked degree of sinusitis, and would seem to be candidates for sinus surgery.

In the third group, in which lobectomy and sinus surgery have both been performed, none of the 11 patients are absolutely symptom-free so far as the chest is concerned. Seven, however, have only a slight amount of sputum, and 2, although still raising sputum, have shown a considerable improvement in the amount. In 2 cases there has been no change so far as the chest is concerned, but the nose and sinus condition has been improved. It is interesting that some of these patients had sinus surgery before their lobectomy. Although their nasal symptoms were much improved, no marked change occurred in the chest until after the lobectomy. It would seem that in this group the bronchiectasis must be considered as simply another locus of infection or, as Dr. E. D. Churchill says, "another sinus."

In the fourth group, that of sinus surgery only, 3 of the 30 patients became symptom-free for two or three years after the operation. They were adults and their cases had been diagnosed as early bronchiectasis; they had a minimum number of chest symptoms before the operation. Thirteen patients showed considerable improvement in the amount of sputum, 4 were slightly improved and the rest were unchanged.

SUMMARY

Sinusitis is a common accompaniment of bronchiectasis.

It may be present at the onset of the chest infection, or may appear, or at least be recognized, later when it is a vital factor in the patient's disability.

Cases of bronchiectasis suitable for lobectomy but uncomplicated by sinusitis show the best end results.

Patients with sinusitis may have considerable sputum from the upper respiratory tract even after the chest has been operated on.

Patients unsuitable for lobectomy have been improved locally, and in some cases where the bronchiectasis is mild the chest symptoms also have been lessened. It is not suggested that sinus surgery will be followed by an eradication of the bronchiectatic cavity: it is not an alternative to lobectomy when the latter is advisable.

330 Dartmouth Street

REFERENCE

1. Goodale, R. L.: Analysis of seventy-five cases of bronchiectasis from the viewpoint of sinus infection. *Ann. Otol., Rhin. & Laryng.* 47:347-359, 1938.

PATHOGENESIS OF PRIMARY AND REINFECTION TYPES OF PULMONARY TUBERCULOSIS*

ESMOND R. LONG, M.D.†

PHILADELPHIA

TUBERCULOSIS resulting directly from first infection with tubercle bacilli, and tuberculosis as it commonly occurs years after a first infection has taken place and healed, are so different that a classification of the disease taking into account the variation in origin, development and character in these two types is necessary.

The two forms have been defined with great care in *Diagnostic Standards*, a manual published by the National Tuberculosis Association that summarizes the classification of tuberculosis and certain technical procedures used in its detection. In early editions the terms "childhood-type tuberculosis" and "adult-type tuberculosis" were used, but in a later one, presenting a classification designated as tentative, these terms were abandoned in favor of the more specific labels "primary tuberculosis" and "reinfection tuberculosis." This

change was logical because with the passage of years and the diminishing incidence of tuberculosis, tuberculous infection is becoming less common in childhood, and first infection with tubercle bacilli correspondingly commoner in the years of adolescence and adult life. In the most recent edition (1940) the designation by types is omitted, and primary and reinfection "phases" are distinguished, a change seemingly intended to avoid the previously implied distinction of virtually separate diseases.

In this manual, primary tuberculosis is described as follows: The disease begins as a single or, more rarely, multiple parenchymal lesion in the lower-lung or middle-lung field, with involvement of the hilar lymph nodes. Encapsulation and calcification constitute the prevalent type of retrogression, and lymphatic and hematogenous dissemination, or spread by direct continuity, the prevalent type of progression. Reinfection-type tuberculosis, on the other hand, is pictured in the

*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 21, 1940.

†Professor of pathology, University of Pennsylvania; director, Henry Phipps Institute, University of Pennsylvania.

following manner: The initial lesion is a parenchymal focus, usually in the upper third of the lung, without gross involvement of the hilar lymph nodes. Retrogression commonly occurs by resorption and fibrosis. Progression takes place by caseation, liquefaction, excavation and bronchogenic spread.

There is no disagreement on the anatomic character and clinical course of primary and reinfection-type tuberculosis in so far as they occur typically in children and adults, respectively. There is divergence of opinion, however, in other important respects. Dispute centers largely on the following questions: the character and prognosis of primary tuberculosis in adolescents and young adults, the source of infection in reinfection-type tuberculosis in adults, and the role of allergy and immunity in the pathogenesis of reinfection-type tuberculosis.

First-infection tuberculosis, as it occurs typically in children, is obviously exogenous. We may dismiss almost without comment the question of the type of tubercle bacillus concerned. Virtually without exception in the United States, where bovine tuberculosis has been almost eradicated, infection is with human-type tubercle bacilli. It is usually not grave in children, although this statement requires some qualification with regard to Negro children. In the latter, as in white children, in the great majority of cases first infection does not lead to progressive disease; however, lesions that do progress are commoner in Negro than in white children, and greater caution is necessary in the former in estimating prognosis and prescribing treatment when early lesions of first infection are discovered. In both white and Negro children the lesion may occur in any part of the lung, and usually, when the infection is sufficiently intense to be represented by a shadow easily seen in the x-ray film, the tracheobronchial lymph nodes are enlarged. If necrosis of tissue in the lesions of the lung and lymph nodes occurs, the recovery which typically follows is accompanied by calcification of the injured area. In the relatively uncommon cases where the disease progresses, it does so by expanding infiltration of the lung, by ulceration of a tuberculous lesion of a lymph node into a bronchus, with tuberculous pneumonia in the lung parenchyma of the tributary bronchial branches, or by vascular involvement leading to generalized tuberculosis.

In adolescents and adults, on the other hand, first infection with tuberculosis does not appear to follow any well-recognized pattern. Indeed, the claims of various investigators as to the type of response can hardly be reconciled. Some assert

that in anatomical character and clinical course, in which it is generally benign, primary tuberculosis in adults is quite like that in children. Others state that the disease is anatomically like that typical of first-infection tuberculosis in children, but that the lesions are more prone to be progressive. A third group holds that the disease anatomically is unlike that characteristic of primary tuberculosis in childhood, having a tendency to conform with the typical reinfection tuberculosis in adults, but that it is clinically of the same benign, non-progressive character that is the rule in children. A fourth group does not agree with any of the others, insisting that primary tuberculosis in adults is both anatomically and clinically unlike first infection in children, resembling reinfection-type tuberculosis in its tendency to apical pulmonary infiltration without involvement of the lymph nodes, and exhibiting a strong tendency to progressive extension with unfavorable outcome.

Knowledge of the truth is of great importance in view of the inescapable fact that primary tuberculous infection in adults, once rare because of the near universality of exposure in early life, is now becoming common. Perhaps a partial answer to the question lies in the fact that in spite of the present frequent postponement of first infection to late years, no unusual incidence of acute or progressive tuberculosis has become apparent. More studies on the subject are desirable. One such, under way at the moment at the Henry Phipps Institute, has disclosed that all the possible varieties of first-infection tuberculosis in adolescents or adults listed above may occur, and indeed that there may be a number of sub-varieties, but that in the limited material available there has been no indication of a preponderance of any one type.

The second disputed problem in the list enumerated above is the source of infection in the characteristic reinfection-type tuberculosis of adults. Up to a decade and a half ago the view most widely held was that this form of tuberculosis is endogenous, the bacilli concerned in the progressive lesion of middle life being mobilized, as a result of some one of a variety of strains, from a previous latent but unhealed lesion of primary type contracted many years before. The last fifteen years have witnessed a sharp reversal of this concept, and wide adoption of the view that reinfections are like first infections in that they are acquired from without, the exogenous superinfection overcoming whatever increased resistance to small doses of tubercle bacilli was conferred by the original or any subsequent non-progressive infection.

A large amount of evidence for this etiology has been brought forth. The well-known studies of Opie and McPhedran¹ have shown that the anatomically characteristic reinfection-type tuberculosis develops much more frequently in previously healthy people in contact with open cases of tuberculosis than it does in previously healthy people not in contact with open cases, even though the two groups may be alike with respect to the possession of old healed lesions of first-infection-type tuberculosis.

On the other hand, because of the increasingly common serial use of x-ray films in cases detected in the early stages of primary infection and followed for years, with final observation at necropsy, evidence is accumulating that characteristic primary lesions may develop, smolder for years with occasional small extensions to other parts of the lungs, and finally mature as progressive tuberculosis of the anatomical type commonly accepted as being of reinfection character. Sweany,² in particular, has written of such cases.

Proof of endogenous development of reinfection-type tuberculosis years after the acquisition of primary tuberculosis is almost impossible, because the possibility of subsequent infection can almost never be ruled out. On the other hand, the abrupt transition from health to progressive disease in patients in contact with open tuberculosis and judged previously to have been infected, because of the presence of calcified lesions or a positive tuberculin reaction of some years' standing, is common, and is convincing for exogenous infection. Some of the best examples have come from the study of tuberculosis in married couples, where a healthy person, with evidence of old healed tuberculosis, develops fresh active disease shortly after marriage to a patient with open tuberculosis.

Evidence against the theory of endogenous development is accumulating in the repeated demonstration that the old foci of primary tuberculosis after dense fibrosis and calcification have occurred no longer contain viable tubercle bacilli (Feldman and Baggenstoss³). The just claim has been made, however, that small lesions secondary to the main primary lesion are numerous, and it is impossible to examine all of them for sterility (Pinner⁴). However, it seems unlikely that the main lesion would heal completely and minor ones remain infectious. On the whole, the distinction between endogenous and exogenous reinfection seems to resolve into that between slowly and often very irregularly progressive primary tuberculosis, often lasting years before it leads to clinical disability, and

fresh disease of abrupt onset resulting from new infection from an outside source.

The difference in anatomic character between primary tuberculosis and reinfection tuberculosis, as they are ordinarily observed in children and adults, respectively, is great. The latter type arises almost exclusively in the upper part of a lung, whereas the former may take origin in any part. In the ordinary reinfection tuberculosis of white persons the hilar lymph nodes are not grossly involved, even when the disease has invaded most of the lung parenchyma. Microscopic involvement of these nodes occurs almost constantly, however, and an exception to the rule occurs in Negro patients; in them, even when the reinfection character of the lesion is thoroughly established by the presence of an unmistakable healed primary tuberculous lesion, gross involvement of the hilar nodes is not uncommon.

Attempts have repeatedly been made to explain the difference in anatomic response in primary and reinfection tuberculosis on immunological grounds. The first infection takes place in tissue not sensitized by the previous presence of tubercle bacilli. The phenomenon of allergy is absent. In reinfection tuberculosis, on the other hand, tubercle bacilli, present long before, have sensitized the tissue. Infection under the two conditions has been likened to experimental skin tuberculosis in normal and previously infected guinea pigs. In these animals in the one case an indolent process occurs, not very conspicuous in the first few days, but spreading slowly and ultimately involving the regional lymph nodes, while in the other there is an explosive reaction with ulceration, the so-called "Koch phenomenon," with less tendency to involve the tributary lymph nodes. The excavation of reinfection tuberculosis has by some been considered as analogous to the ulceration of the latter.

Actually, however, the resemblance in the two cases is rather remote. Tuberculous infection of the skin of normal guinea pigs, while slow in evolution, is progressive in development, whereas first infection in children commonly progresses for a few months and then regresses. Its relations to allergy are complicated. Absent in the beginning, allergy develops a few weeks after infection, while the lesion is progressive. It appears to reach its peak about the time of maximum development of the lesion (Johnston, Howard and Maroney⁵), and to recede as the latter regresses. It is difficult to distinguish which is cause and which effect, however. Certainly tuberculosis is still active in a stage when strong allergy is pres-

ent, and the latter has no tendency to convert the lesion to excavating tuberculosis characteristic of the reinfection type.

Allergy in the ordinary sense of increased tissue reactivity cannot explain the difference between the primary and reinfection types of tuberculosis. In moderately advanced pulmonary tuberculosis allergy is depressed, and yet new lesions forming in the progressive course of the disease have the same fibroulcerative character as have the first lesions of reinfection. The key phenomenon in progressive reinfection-type tuberculosis is liquefaction. Formerly this was explained as being due largely to secondary infection and the proteolytic ferments of the bacteria or the leukocytes attracted by them. However, recent research (Pagel⁶) suggests that it is an independent phenomenon, related in some way to the immunologic state. An Arthus-like phenomenon, dependent on reaction between the caseated tissue, which is in effect a foreign tissue, and plasma antibodies, is postulated by certain investigators (Pagel,⁶ Lurie⁷), but clear proof for such a phenomenon is lacking.

In such cases there is always satisfaction in falling back on objective facts, which appear in this case to be as follows: Reinfection-type tuberculosis, regardless of allergy, is usually non-progressive. The majority of reinfections are small, are met by adequate tissue response and heal. A certain number, presumably those dependent on excessive dosage, are progressive. Liquefaction is the most significant pathologic process in progression. Bacilli are numerous in liquefying regions (Long⁸), and drainage of liquefying areas results at the same time in excavation and bronchogenic spread to previously healthy parts of the lungs, where the sequence may be repeated. If the liquefaction process occurring in caseous tuberculous tissue were understood, the nature of progressive tuberculosis would be more nearly apparent.

The subject cannot be dismissed without some reference to the difference between allergy and immunity. There is evidence that allergy may be abolished by desensitization, while increased resistance to infection persists (Rich⁹), and also that allergy may wane with healing while increased resistance remains independently. The question may be raised if the latter, rather than allergy, determines the anatomic character of reinfection-type tuberculosis. This can be answered only by observation of the character of tuberculosis that develops on reinfection in previously infected persons who have lost their allergy. Cases like this have been observed, but no

uniformity in the anatomic character of the reinfection is apparent. Israel and Long¹⁰ have seen tuberculosis of three different types develop in patients previously infected primarily who subsequently lost their allergic sensitivity, namely, a lesion quite like typical primary tuberculosis in children, tuberculous infiltration of the type characteristic of reinfection in adults, and pleurisy with effusion.

Finally, the relation between the anatomic character of reinfection tuberculosis and age must be considered. In the past, primary tuberculosis has occurred in children and reinfection tuberculosis in adults. It is a fair question whether primary tuberculosis, if it occurred in adults, might not take on the character of reinfection tuberculosis at the same age. This possibility has already been discussed. A number of investigators have recorded that in their experience primary pulmonary tuberculosis in adults tends to be apical in location with little tendency to affect the tracheobronchial lymph nodes.

It is evident that a good deal more research is necessary for the explanation of the anatomic difference between primary and reinfection tuberculosis. The relations to age are now subject to investigation, since so much first infection now occurs at a period of life in which reinfection tuberculosis is common. If a relation to an immunity that outlasts allergy exists, that, too, should be discovered, since today there are many persons, once infected, who have lost their allergy, through subsidence of the original lesion and lack of subsequent reinfection, and who may yet meet infections of serious intensity.

SUMMARY

There is no disagreement on the anatomic character and clinical course of primary and reinfection tuberculosis as they occur typically in children and adults respectively. There is disagreement, however, on the character of primary infection as it occurs in adults. It is evident that the latter does not always conform to the characteristic picture of first-infection tuberculosis in childhood, but may assume a variety of forms. It is a problem of future research to determine which is the commonest.

Reinfection-type tuberculosis may be either exogenous or endogenous. The exogenous character is more readily susceptible of demonstration than is the endogenous. The frequent abrupt onset of upper-lobe tuberculosis in a person long previously tuberculin-positive and a short time previously in contact with an open case of tuberculosis is acceptable proof for exogenous invasion. Endogenous

pulmonary tuberculosis is chiefly progressive primary tuberculosis, rather than abrupt metastatic tuberculosis dependent on the existence of an old unhealed primary focus.

The anatomic character of reinfection tuberculosis is not necessarily a function of allergy. Allergy is present in the mid-stages of primary tuberculosis, without influencing its course in the direction of reinfection-type tuberculosis. The characteristic feature of progressive reinfection tuberculosis is liquefaction. The latter is the key problem of progressive tuberculosis, and appears to be largely independent of the allergic state, in the accepted sense of the term, although it is probably connected in some way with the immunologic state of the infected person.

7th and Lombard Streets

REFERENCES

1. Opie, E. L., and McPhedran, F. M.: Contagion of tuberculosis. *Am. Rev. Tuberc.* 14:347-419, 1926.
2. Sweeney, H. C.: Pathology of primary tuberculous infection in the adult. *Am. Rev. Tuberc.* 39:236-255, 1939.
3. Feldman, W. H., and Baggenstoss, A. H.: Residual infectivity of primary complex of tuberculosis. *Am. J. Path.* 14:473-490, 1938.
4. Pinner, M.: Pneumonitis. *Am. Rev. Tuberc.* 38:730-737, 1938.
5. Johnston, J. A.; Howard, P. J., and Maroney, J.: Quantitative study of tuberculin reaction in childhood tuberculosis. *Am. Rev. Tuberc.* 29:652-659, 1934.
6. Pagel, W.: Studien über tuberkulöse Erweichung. *Beitr. z. Klin. d. Tuberk.* 76:414-458, 1931.
7. Lurie, M.: unpublished data.
8. Long, E. R.: From pathology to epidemiology in tuberculosis: softening of caseous tubercle and its results. *J. A. M. A.* 104:1883-1888, 1935.
9. Rich, A. R.: Immunity in tuberculosis. New York Academy of Medicine's *Diseases of the Respiratory Tract*. 418 pp. Philadelphia: W. B. Saunders Co., 1936. Pp. 215-239.
10. Israel, H. L., and Long, E. R.: Primary tuberculosis in adolescents and young adults. *Am. Rev. Tuberc.* (in press).

DISCUSSION

DR. HENRY D. CHADWICK, Waltham: Dr. Long has stated some of the problems in the pathology of tuberculosis that have been the subject of intensive research by many investigators. Where there is a difference of opinion a clinician may venture to give his impressions, based on observing the behavior of the disease in living subjects. Allergy or sensitivity of the tissues to the presence of the tubercle bacillus develops uniformly following infection, regardless of the age of the individual at the time the infection takes place.

The opportunities for such infections have lessened with the decline in tuberculosis. Since 1900 in Massachusetts the drop in the death rate has been 86 per cent. The incidence of infection is only about half of what it was fifteen years ago. Instead of 40 per cent of high-school students reacting to the tuberculin test only about 20 per cent now do so. This means that 80 per cent of the young people now enter adulthood free from infection. If they become infected afterward they develop primary tuberculosis, or what was formerly called the childhood type.

It is my opinion that the course followed by primary tuberculosis in these cases is not modified except in so far as immunity or resistance is influenced by age. We could express this by saying that the course of primary tuberculosis is dependent on the degree of immunity that is present in an individual at the time the bacillus is implanted. Resistance, however, varies with age. In infancy there is a high degree of susceptibility, and infection occurring in the first and second years of life often results in meningitis or generalized tuberculosis. At from three to ten years of age, resistance is at its highest point. Through adoles-

cence into young adult life susceptibility again seems to increase, as is shown by the climbing death rate, especially in women. After the thirtieth year the deaths in men show a preponderance and the rate for them steadily increases, reaching its peak in the sixties and seventies.

Reinfection tuberculosis doubtless occurs as a result of both endogenous and exogenous infection. I am one of those who believe that the former is the more usual source, and in support of this contention submit the following evidence. A study by Dr. Pope of 850 cases of primary tuberculosis found in the Massachusetts schools in 1924-1928 and reviewed in 1932 showed that 30, or 3.7 per cent, had developed the reinfection type of pulmonary tuberculosis. In a control group of 405 positive reactors of similar age, sex and family contact but without roentgenological evidence of disease at the time of first examination, 3, or 0.7 per cent, developed pulmonary tuberculosis. Thus there were two groups of infected children: one with lesions massive enough to be demonstrated by x-ray, the other with no visible lesions. The former group developed five times as many cases of reinfection tuberculosis as did the latter. The natural inference is that most of them were reinfected from their own foci of disease, as otherwise the two groups were subjected to similar environmental conditions. Again, the average age of men admitted to sanatoriums for treatment is increasing. At the Middlesex County Sanatorium the men admitted during the three years prior to 1939 were on an average five years older than those admitted for a similar period prior to 1935. There are fewer cases of tuberculosis in the State and 4500 of them are hospitalized, thereby keeping that number of foci of infection from spreading the disease in the community. The death rate is declining at the rate of 40 per cent in each decade. Yet the mortality for men from sixty to seventy remains high—in fact it is higher than at any other age period. This must mean that resistance becomes lower with advancing years, and that men fall victims to their own tuberculous focus that they have been harboring for years—probably acquired in childhood. This represents the carry-over from a time when infection with tubercle bacilli was more nearly universal. Otherwise how can we account for the steady climb of the death rate from tuberculosis for the United States in 1937 from 33 per 100,000 in the age group fifteen to nineteen to 104 for the age group seventy-five to seventy-nine, notwithstanding the fact that opportunities for exogenous infection have steadily decreased.

Tuberculosis is a lifetime disease in many cases, with periods of latency alternating with more or less active phases extending over many years. The thing called "resistance" waxes and wanes, and in doing so influences the parasitic existence of the tubercle bacillus; for the host this means varying degrees of health and illness or death. Dr. Long says, "The key phenomenon in progressive reinfection tuberculosis is liquefaction" but acknowledges it is "a process that is not understood." In a few very susceptible individuals the diseased lung is seen literally to melt away as the course of the disease is followed with serial x-ray films.

This type of patient is seen less frequently as the years pass. The breed seems to be dying out and a tougher strain survives. Something seems to be lacking in such individuals which makes one ask whether or not tuberculosis should be classed as a deficiency disease. Some gauge by which resistance can be measured is needed, and some substance or vitamin not yet discovered that can be used to fortify those who are deficient in this essential element, in order to increase their immunity to a degree that will withstand infection.

THE TREATMENT OF PNEUMOCOCCAL PNEUMONIA*

FRANCIS G. BLAKE, M.D.†

NEW HAVEN, CONNECTICUT

IT IS a familiar fact that the treatment of pneumococcal lobar pneumonia has been revolutionized within the short period of three years, first by the introduction of the type-specific antipneumococcus rabbit serums by Horsfall, Goodner, MacLeod and Harris,¹ and shortly thereafter by the introduction of sulfapyridine by Whitby.² More recently a new sulfonamide derivative, sulfathiazole,³ has appeared. This compound, reported by McKee, Rake, Greep and van Dyke⁴ to be as effective as sulfapyridine in experimental pneumococcal infections, is now being submitted to trial in many clinics. The efficacy of antipneumococcus rabbit serum and of sulfapyridine, either alone

New Haven Hospital with sulfathiazole will be briefly presented.

CLINICAL MATERIAL AND METHODS

The clinical material which forms the basis for this analysis consists of 250 cases of pneumococcal lobar pneumonia treated at the New Haven Hospital between November 30, 1938, and May 1, 1940. Of these, 109 up to January 2, 1940 (Table 1), were treated with sulfapyridine² alone and 41 with sulfapyridine and antipneumococcus serum, and 100 between November 30, 1939, and May 1, 1940, with sulfathiazole,³ of which 3 also received serum therapy (Table 2). In the group of 150

TABLE 1. Data on Cases of Pneumococcal Lobar Pneumonia Treated with Sulfapyridine and with Sulfapyridine and Antipneumococcus Serum.

TYPE OF PNEUMOCOCCUS	SULFAPYRIDINE			SULFAPYRIDINE AND SERUM			TOTAL		
	NO OF CASES	BLOOD CULTURE POSITIVE	DEATHS	NO OF CASES	BLOOD CULTURE POSITIVE	DEATHS	NO OF CASES	BLOOD CULTURE POSITIVE	DEATHS
1	17	5	1	17	6	2	34	11	3
2	0	0	0	4	2	1	4	2	1
3	25	0	4	1	0	1	26	0	5
4-8	31	2	1	17	6	2	48	8	3
9-13	5	1	0	0	0	0	5	1	0
14	14	1	1	1	1	1	15	2	2
15-32*	17	0	0	1	0	0	18	0	0
Totals	109	9	7	41	13	7	150	24	14
Percentages		8	6		37	17		16	9

*Including higher types not determined

or combined, in individual patients, particularly when treatment is initiated early, is well known. Furthermore, sufficiently extensive and consistent statistical data have already been published⁵⁻⁷ to establish the fact that these methods of treatment possess remarkable curative value, bringing about a notable lowering of case-fatality rates. Consequently it is not the major purpose of this paper to provide further statistical evidence in support of these facts, but rather to discuss some of the problems encountered in the treatment of patients, with particular emphasis on the variations in clinical response which occur. An attempt will be made to analyze some of the factors involved in these variations, and finally our recent experience at the

patients receiving sulfapyridine there are included 45 under thirteen years of age treated on the Pediatric Service prior to June, 1939. All other patients were over thirteen. No cases have been excluded, whether moribund on admission to the hospital and dying within less than twenty-four hours (5 cases), or dying of some other disease after recovering from pneumonia (3 cases). Comparison of the groups is not statistically valid because of the small numbers and lack of equivalence in the many variables involved, particularly with respect to age distribution and the incidence of severe bacteremic cases.

In general the initial dose of sulfapyridine used at first in the adult patients was 2 gm., as recommended by Evans and Gaisford.⁸ Later an initial dose of 4 gm., usually divided into four doses of 1 gm. each at hourly intervals, was used. The

*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 21, 1940.

†From the Department of Internal Medicine, Yale University School of Medicine, and the Medical Service, New Haven Hospital.

Aided by a grant from the Fluid Research Fund of Yale University School of Medicine.

†Sterling Professor of Medicine, Yale University School of Medicine, physician-in-chief, New Haven Hospital.

²The sulfapyridine used was in large part obtained through the courtesy of Merck and Company, Rahway, New Jersey.

³The sulfathiazole used was largely supplied through the courtesy of E. R. Squibb and Sons, New York City, and in part by Merck and Company.

initial dose was followed by 1 gm. every four hours day and night. Appropriately smaller doses were used in infants and children. With sulfathiazole an initial single dose of 4 gm. followed by 1 gm. every four hours was employed. Variations from this general scheme of dosage have been based primarily on blood concentrations outside the usual range, or on other factors, such as persistent vomiting. This scheme has seemed therapeutically effective and has served to establish promptly in the majority of patients a blood concentration ranging between 4 and 10 mg. per 100 cc. Parenteral treatment has been resorted to when

CLINICAL RESPONSE TO THERAPY

Obviously the major problems involved at present in the treatment of patients with pneumococcal pneumonia are, first, the choice between serum therapy and chemotherapy; next, decision whether and when combined therapy should be employed; and lastly, if chemotherapy is chosen, whether sulfapyridine or sulfathiazole should be used. Answers to these problems would appear to be still in the realm of opinion based on individual experience, rather than backed by sound statistical evidence. For this reason the opinions expressed below should be regarded as tentative and sub-

TABLE 2. *Data on Cases of Pneumococcal Lobar Pneumonia Treated with Sulfathiazole and with Sulfathiazole and Antipneumococcus Serum.*

TYPE OF PNEUMOCOCCUS	SULFATHIAZOLE			SULFATHIAZOLE AND SERUM			NO. OF CASES	TOTAL	
	NO. OF CASES	BLOOD CULTURE POSITIVE	DEATHS	NO. OF CASES	BLOOD CULTURE POSITIVE	DEATHS		BLOOD CULTURE POSITIVE	DEATHS
1	30	7	1†	2	2	2†	32	9	3†
2	1	0	0	0	0	0	1	0	0
3	17	2	1	1	0	0	18	2	1
4-8	21	6	0	0	0	0	21	6	0
9-32*	28	0	0	0	0	0	28	0	0
Totals	97	15	2	3	2	2	100	17	4
Percentages								17	4

*Including higher types not determined.

†Bacteremic.

severe vomiting has interfered with adequate oral dosage and in stuporous or extremely ill patients. In adults treatment has ordinarily been continued until the seventh to the ninth day of the disease; in children it was commonly stopped by the fifth day.

In the sulfapyridine-treated group, serum therapy was combined with chemotherapy in 41 cases, the serum usually being given as soon as the type of pneumococcus was determined, in a single dose or in two divided doses totaling 100,000 to 300,000 units, depending on the duration and estimated severity of the disease and the type of pneumococcus, according to the plan outlined by Loughlin, Bennett and Spitz.⁹ As time went on serum was reserved more and more for the late or obviously very severe cases. In the sulfathiazole-treated group it was used only three times.

For purposes of subsequent analysis, all patients had an initial blood culture and the majority one or more subsequent cultures. Daily determinations of the concentrations of total and free sulfapyridine or sulfathiazole were made in most of the cases. The blood was watched closely for evidences of neutropenia and anemia, the urine for hematuria. A careful record of nausea and vomiting and other untoward reactions was kept.

ject to modification through the experience of others or further experience of our own.

While it may be generally agreed that the clinical response of patients with lobar pneumonia to treatment with antipneumococcus serum or chemotherapy is in general excellent, it is nevertheless quite variable, and it is these variations from patient to patient that will be discussed as a background for the opinions to be expressed. Since the clinical material dealt with is variable with respect to certain determinable factors such as type of pneumococcus, age, day of disease when treatment was started and presence or absence of bacteremia, the possible influence of these on variations in clinical response will be analyzed. In the analysis the toxic reaction of nausea and vomiting will be disregarded. The problems presented by this and other untoward reactions to serum or sulfonamide compounds will be analyzed separately. The response to therapy will be divided into initial response and subsequent course. The data are summarized in Tables 3, 4 and 5.

Patients Treated with Sulfapyridine Alone

The most frequent type of clinical response encountered in the 109 patients treated by sulfapyri-

dine alone (Table 3) was recovery by crisis within approximately twenty-four hours after initiation of treatment and an uneventful convalescence, occurring in 55 cases (50 per cent). The second type of response was prompt recovery by rapid lysis within forty-eight hours and an uninterrupted convalescence; this occurred in 14 cases (13 per cent). In these two groups, totaling 63

TABLE 3. *Variations in Clinical Response Shown by Patients Treated with Sulfapyridine Alone.*

INITIAL RESPONSE	SUBSEQUENT COURSE	NO. OF CASES	PER CENT
Recovered cases			
Crisis	Convalescence uneventful	55	50
Lysis	Convalescence uneventful	14	13
Crisis or lysis	Low fever, 2 to 10 days	12	11
	Relapse	4	4
	Infectious complication	3	3
	Toxic drug reaction	13*	12*
None	Toxic drug reaction	1	1
		102	94
Fatal cases			
Crisis	Agranulocytosis	1	1
Temporary or none		0	5
		7	6

*Plus 4 cases in other groups 17 (16 per cent)

per cent, the response may be said to have been highly satisfactory and to have offered no particular problems. Obviously the addition of serum therapy was not indicated.

The third type of response consisted of an initial rapid improvement by crisis or lysis, followed by a low-grade fever ordinarily ranging between 100 and 101°F. (rectal) for a few days to a week or more without apparent cause. Ultimate recovery occurred without any infectious complication or delayed reaction to the drug. There were 12 cases in this group. They represent a type of case which must be carefully watched and is sometimes puzzling.

Another variation in clinical course following apparent initial recovery was relapse, with fever and physical signs indicating spread of the pneumonia. This occurred in only 4 cases: in 1 after two days of normal temperature while the patient was still under treatment; in 3 following discontinuance of sulfapyridine. The major problem presented by this occurrence is that of distinguishing between relapse of infection and drug fever. Our experience indicates that, unless it can be proved otherwise, the sudden recurrence of fever after a few days of essentially normal temperature should be tentatively regarded as drug fever and chemotherapy should be stopped.

In 3 cases apparent convalescence was interrupted by an infectious complication. These were

a sterile serofibrinous pleural effusion of ten days' duration, requiring drainage by thoracentesis, an organizing pneumonitis and lung abscess associated with a superimposed staphylococcal infection, and an empyema requiring surgical drainage. All the patients recovered.

Still another variation in clinical course following a satisfactory initial response was that due to untoward reactions to sulfapyridine itself. This occurred in 13 cases with an otherwise uneventful subsequent course, and in 4 which are included in other groups, making a total of 17 cases (16 per cent). These are discussed further below.

Only 1 patient (aged sixty-three, Type 3, treated on seventh day) in the recovered group showed no apparent initial response, perhaps because of the prompt development of hepatitis, followed by drug fever with rash.

The final group consists of 7 fatal cases (6 per cent). One of these patients, a woman of sixty-one with advanced Paget's disease and a Type 4 pneumococcus pneumonia, recovered promptly from the pneumonia but subsequently developed agranulocytosis on the twenty-second day, from which she died three days later. The data on the other 6 fatal cases are as follows:

M. S., aged 70; arteriosclerotic heart disease, asthmatic bronchitis and emphysema; treated on 5th day; Type 1, bacteremic; died 10th day.

A. A., aged 83; treated on 4th day, Type 3, bilateral; died 7th day.

I. K., aged 74; arteriosclerotic heart disease; treated on 5th day; Type 3, bilateral; died 9th day.

J. P., aged 55; arteriosclerotic heart disease and congestive failure; treated on 6th day; Type 3, bilateral; died 12th day.

J. L., aged 75; severe bleeding peptic ulcer; treated on 2nd day; Type 3; died 7th day.

S. D., aged 67; arteriosclerotic heart disease and congestive failure; treated on 4th day; Type 14, moribund; died 5th day.

The obviously noteworthy fact is that there were no deaths in patients under fifty-five years of age, and that fatalities occurred for the most part among those who suffered from severe chronic disease.

Analysis of the relation of the type of pneumococcus to the variations in clinical response shows a significant difference only in the case of Type 3 infections. While the percentage of all other types showing prompt clinical recovery by crisis or lysis (inclusive of those with toxic drug reactions) ranged from 82 to 86, it was only 48 per cent in the Type 3 cases. Consequently the percentage of Type 3 patients showing low-grade fever following an initial favorable response, relapse or death

was considerably higher than it was in the other types. That this apparent relative ineffectiveness of sulfapyridine is due to a greater resistance to the action of sulfapyridine on the part of the Type 3 pneumococcus seems improbable, however, when the relation of age to clinical response is analyzed and it is at the same time noted that 64 per cent of the Type 3 cases were over fifty years of age.

The influence of age on the clinical response of patients with pneumococcal lobar pneumonia treated with sulfapyridine is important. It is illustrated by the fact that 97 per cent of patients under ten, 75 per cent of those from ten to thirty-nine, 68 per cent of those from forty to fifty-nine, and 48 per cent of those sixty or older recovered by crisis or lysis, with uneventful convalescence apart from drug reactions. Conversely the proportion showing low-grade fever, relapse, complications or fatal outcome steadily rose with increasing age, the figures being 3 per cent under ten years, 25 per cent from ten to thirty-nine, 32 per cent from forty to fifty-nine, and 52 per cent in patients of sixty or over, all the deaths being in patients of fifty-five or over.

The influence of delayed treatment is less conspicuous. Of 69 cases in which treatment was started on or before the third day of the disease, 77 per cent showed prompt recovery by crisis or lysis (including those with toxic drug reactions). Of 40 cases in which treatment was begun on the fourth day or later, the percentage was approximately the same, 73. While it is true that the case fatality rate was only 1 per cent in the cases treated early, as contrasted with 15 per cent in those treated late, it must be pointed out that slightly less than one quarter of the early cases were over fifty years of age, as compared with nearly half the late cases.

In this series the influence of bacteremia appears unimportant, but the number of bacteremic cases is too small to warrant analysis. Six of the 7 patients recovered, the fatal case being a Type 1 pneumonia in a man of seventy, admitted on the fifth day of the disease.

Patients Treated with Sulfapyridine and Antipneumococcus Serum

The variations in clinical response to combined therapy—sulfapyridine and antipneumococcus serum—were in general quite similar to those in patients treated with sulfapyridine alone, with the addition of serum disease, which occurred in approximately one third of the cases. The data are summarized in Table 4, from which it will be seen at once that while a much lower proportion of patients recovered promptly and uneventfully than

was the case in the patients treated with sulfapyridine alone, a much higher proportion presented complications or died.

The complications encountered in this group were as follows: sterile pleural effusion (1 case); empyema (4 cases); organizing pneumonitis with abscess (2 cases); thrombophlebitis (1 case); and possible cerebral arteritis with hemiplegia (1 case). All the patients recovered except one of those with empyema. With one exception, a patient of thirty-

TABLE 4. *Variations in Clinical Response Shown by Patients Treated with Sulfapyridine and Antipneumococcus Serum.*

INITIAL RESPONSE	SUBSEQUENT COURSE	NO. OF CASES	PER CENT	TOTAL PER CENT
Recovered cases				
Crisis or lysis	Convalescence uneventful	11	27	
	Low fever, several days	4	10	(+3) 17
	Toxic drug reaction	2	5	(+1) 7
	Serum disease	7	17	(+6) 32
Temporary improvement	Infectious complication	8	20	(+1) 22
None to serum	Recovered with sulfapyridine	1	2	
None to sulfapyridine	Recovered with serum	1	2	
		34	83	
Fatal cases				
Crisis or lysis	Died, other disease	2	5	
Temporary or none		5	12	
		7	17	

two with advanced rheumatic heart disease admitted moribund with a Type 1 bacteremic pneumonia, the patients who died were over fifty-eight years of age and subject to more or less severe chronic disease.

While the two groups are comparable with respect to the day of the disease on which treatment was started and in the proportion of patients over fifty, the combined-therapy group included proportionately many fewer children under ten (10 per cent *vs.* 33 per cent) and many more bacteremic cases (37 per cent *vs.* 6 per cent) than did the group treated with sulfapyridine alone. As already pointed out, these differences make comparison invalid.

Patients Treated with Sulfathiazole

There are 100 patients in the sulfathiazole-treated group, including 3 who also received antipneumococcus rabbit serum. The latter are included since serum was not given at once, as was done in nearly all the sulfapyridine-treated group, but later when it seemed possible that sulfathiazole alone would not control the infection.

The data concerning initial response and subsequent course are shown in Table 5, from which it will be seen that they fall into the same categories as do the previous groups. The patients recovering promptly by crisis or rapid lysis with

uneventful convalescence comprised 55 per cent of the group, approximately equivalent to the corresponding percentage in the sulfapyridine treated group. The number of cases showing low fever for several days after the initial satisfactory response is somewhat higher, 26 per cent, undoubtedly owing to the absence of children and the higher proportion of patients over forty years of age (65 per cent *vs* 41 per cent). Relapse occurred in only 1 case, on the tenth day of convalescence, six days after sulfathiazole had been stopped, the patient being

TABLE 5 Variations in Clinical Response Shown by Patients Treated with Sulfathiazole *

INITIAL RESPONSE	SUBSEQUENT COURSE	NO OF CASES	PER CENT
Recovered cases			
Crisis	Convalescence uneventful	37	37
Rapid lysis	Convalescence uneventful	18	18
Crisis or lysis	Low fever 2 to 10 days	26	26
	Temporary relapse	1	1
	Sterile pleural effusion on	4	4
	Toxic drug reaction on	6†	6†
Improved	Gradual lysis	4	4
		96	96
Fatal cases			
Temporary or none		4	4

*One recovered case and 2 fatal cases received antipneumococcus serum
†Plus 1 case in another group 7 (7 per cent)

a boy of eighteen with a Type 16 non bacteremic pneumonia. It was immediately controlled by the resumption of sulfathiazole therapy. Four cases developed sterile pleural effusions sufficiently large to require thoracentesis. Two of the patients who died had empyema. The incidence of toxic drug reactions, which were relatively minor in severity, was about half that in the sulfapyridine treated group. Four patients recovered by gradual lysis over a period of several days.

The number of fatal cases is remarkably small. The data concerning them are as follows:

R. C., aged 46, treated on 2nd day, Type 1, bacteremic, sulfathiazole plus 400,000 units antipneumococcus serum; temporary improvement, serum disease, acute glomerulonephritis, empyema and thoracotomy, died in uremia 39th day.

R. S., aged 50, heart disease with failure, treated on 3rd day, Type 1, bacteremic, sulfathiazole plus 300,000 units antipneumococcus serum, died 66 hours after admission.

R. C., aged 49, advanced hypertensive cardiovascular disease with severe congestive failure, anasarca and cirrhosis of liver, treated on 4th day, Type 1, bacteremic, moribund, died 14 hours after admission.

A. H., aged 62, treated on 15th day, Type 3, non bacteremic, bilateral consolidation, with empyema and superimposed staphylococcal infection of lungs, died 25th day.

Analysis of the relation of the type of pneumococcus to the variations in clinical response shows the same tendency as in the sulfapyridine treated group. For Type 3 cases to recover less promptly than those due to other types (44 per cent *vs* 64 per cent), probably owing to the larger proportion of older patients.

The influence of age on the clinical response to sulfathiazole is comparable to that in the sulfapyridine treated group, 76 per cent of the patients under forty showing prompt recovery by crisis or lysis with uneventful convalescence apart from an occasional drug reaction, as contrasted with 50 per cent of those over sixty. Conversely, the proportion of those showing low fever, slow lysis, complications or fatal outcome rose from 24 per cent in the younger group to 50 per cent in the older one.

The influence of delayed treatment and of bacteremia appears to be somewhat more conspicuous in the sulfathiazole treated than in the sulfapyridine treated group, presumably because of the higher proportion of older patients and severe bacteremic cases. Thus, only 45 per cent of the patients treated with sulfathiazole whose treatment was begun later than the third day of the disease recovered promptly by crisis or rapid lysis, as contrasted with 73 per cent in the sulfapyridine treated group, but 65 per cent of those treated with sulfathiazole were over forty years of age and 17 per cent were bacteremic, against 41 per cent and 7 per cent, respectively, in the sulfapyridine cases.

FACTORS INFLUENCING MORTALITY

A brief analysis of the influence of bacteremia and of age on mortality in the total series of 250

TABLE 6 Relation of Bacteremia to Mortality

TYPE OF THERAPY	POSITIVE BLOOD CULTURE			NEGATIVE BLOOD CULTURE		
	NO OF CASES	DEATHS	MOR TALITY RATE %	NO OF CASES	DEATHS	MOR TALITY RATE %
Sulfapyridine	9	1	11	100	6	6
Sulfapyridine plus serum	15	4	27	26	3	12
	24	5	21	126	9	7
Sulfathiazole	1*	3*	18	83†	1	1

*Two cases received antipneumococcus serum
†One case received antipneumococcus serum

patients is presented in Tables 6 and 7. Careful study indicates that, in this series, old age, with its accompanying greater incidence of chronic disease, was a more potent factor than was bacteremia. This is well illustrated in the total column in Table 7, in which it will be noted that only

OSTEOMYELITIS OF THE COCCYX AND SACRUM WITH SINUS FORMATION SIMULATING ANORECTAL FISTULA*

Report of Two Cases

HARRY E. BACON, M.D.,† AND ANDREW TAYLOR, M.D.‡

PHILADELPHIA

INFECTIONS of the perineum are surgical conditions of common occurrence, which, in an age of certified specialization, may be seen by any one of several types of specialist. They include rare abscesses, pointing in the perineum, from ruptured appendices,¹ and caries of the pelvic bone.²⁻⁴ It is the purpose of this paper to present two unusual cases which were cured only after localization of the infective process in the lower portion of the vertebral column.

CASE 1. M. B., a 17-year-old Negress, was admitted to the Proctologic Service of Temple University Hospital on November 30, 1938, with a provisional diagnosis of tuberculous fistulas. The patient described a creamy discharge from the anal region of 5 months' duration. Prior to admission she was treated by "needles" by her family physician. The rest of the history was irrelevant.

Examination showed the presence of two external openings, both posterior to the anal verge and approximately 1 cm. from it; one was located in the midline, and the second slightly to the right. The appearance of the openings was in no way unusual. An area of induration surrounded each, but could not be traced digitally as it seemed to be lost in the tissues of the anococcygeal region. On introducing a probe into each aperture, the direction was toward the coccyx, and the penetration 1 and 2 cm., respectively. Repeated examination of the rectum showed no internal opening or primary lesion. The general physical examination was negative. Roentgenographic study of the chest and the gastrointestinal tract was negative.

The x-ray report of the lumbosacral spine was as follows (Fig. 1):

There is a definite defect in the left side of the fourth sacral segment, and the distal end of the sacrum is eburnated and somewhat irregular in appearance. There has been an osteomyelitis of the sacrum, and it is suspected that this process may still be active. There has been loss of bony substance between the sacrum and coccyx, and the latter is angulated acutely in relation to the sacrum.

Further x-ray study consisted of injection of the sinuses with Lipiodol and fluoroscopic examination, but little or no information was gained except that there was no free communication with the rectum.

The red-cell count was 4,430,000, and the hemoglobin 12.5 gm. The white-cell count was 11,250, with 81 per cent polymorphonuclears, 17 per cent lymphocytes, 1 per

cent eosinophils and 1 per cent basophils. Blood Wassermann, Kolmer, Kahn and Kline tests were negative. A complement-fixation test for gonococcal infection was negative. The sedimentation rate was 11.5 mm. in 1 hour.

With a provisional diagnosis of sacrococcygeal osteomyelitis, resulting in sinus formation simulating ano-



FIGURE 1.

rectal fistulas, operation was performed by one of us (H. E. B.) under Avertin and nitrous oxide anesthesia. By careful probing and injection of methylene blue in Petrolagar, the sinuses were found to extend directly to the coccyx and sacrum. Both tracts were widely excised, and the coccyx and lower sacral segment were removed. The wound was left open and permitted to heal by granulation.

Gross section of the tissue showed no cystic formation. The microscopic report was as follows (Fig. 2):

The epithelium is hyperplastic with increased surface keratinization. The epithelial pegs are distorted and elongated; the corium is thick and sclerotic. There is a perivascular mononuclear cellular infiltration, the predominant cells of which are plasma cells. Some thickening of the vessel walls is noted. Another section of the corium shows chronic granulation tissue with proliferative fibrosis and cellular infiltration. Most of the cells are plasma cells. Sections of bone show some necrosis of the spicules, and infiltration of the marrow with fat and a chronic inflammatory reaction of the periosteum as well as of the bone. There is no

*From the Department of Proctology, Graduate Hospital, University of Pennsylvania, and the Department of Proctology, Temple University Hospital.

†Assistant professor of proctology, Temple University School of Medicine, and Postgraduate School of Medicine, University of Pennsylvania.

‡Formerly, fellow in proctology, Graduate School of Medicine, University of Pennsylvania.

evidence of tuberculous infection. Diagnosis: chronic inflammation and osteomyelitis.

Following operation the wound was packed lightly with dichloramine-T gauze. A heat cradle was employed and ultra-violet light therapy given each day. The patient was discharged to her family physician 17 days after opera-

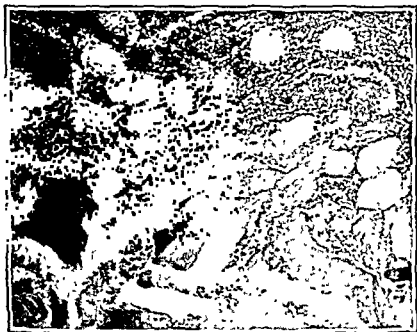


FIGURE 2.

tion. The wound was completely healed 6 weeks later. According to the physician, the patient has offered no complaints.

CASE 2. G.R., a 42-year-old Negro, was seen in the Proctologic Clinic of the Graduate Hospital in May, 1937, at which time he complained of a "boil" on the right side of the anus. He gave a history of having had a low back injury 17 years previously. He had had trouble about the anus for 2 months. One month previously a "boil" opened spontaneously on the left buttock. A diagnosis of horseshoe fistula was made, and operation at that time consisted of incision of the abscess and excision of a portion of a tract on the other side.

Following this procedure the wounds healed, and the patient was free of symptoms until the following October, when he again began to have perianal pain, recurring attacks of swelling and discharge of pus from the perineum. He was readmitted to the hospital in March, 1938. A fistulous tract on the left side was found and excised, but no internal opening was demonstrable.

In April, 1938, the patient was again readmitted because of pain and discharge of pus. An incision through the right tract was made up to the muscle, and a seton of linen thread was inserted through the internal opening and carried over to the right external opening. Two weeks later the patient was readmitted for removal of a fistulous tract. Examination showed two lateral, open, granulating wounds. By this time the course of the disease had aroused suspicion, and the coccyx was x-rayed; it showed "an irregularity in the second coccygeal segment suggestive of a localized osteomyelitis." Operation at this time consisted of fistulectomy from the right to the left internal opening.

Following this operation the patient continued to have intermittent attacks of perianal pain and almost constant discharge until seen in the clinic in January, 1939. General physical examination revealed some changes in the left pulmonary apex suggestive of tuberculosis. X-ray study showed chronic tuberculous changes in both lung fields, with a possible area of activity in the left apex. Local examination of the perineum presented a discharging

sinus on each side of the anus slightly to the posterior phase and marked deformity of the parts, due to extensive scarring. There was tenderness on palpation of the coccyx. The sinuses could be made to exude a watery fluid on pressure over them. A probe when inserted into the tracts passed posteriorly and impinged on bone, but no suggestion of extension toward the rectum or anus was noted.

The urine was negative on three examinations. The sputum was negative for tubercle bacilli on four occasions. The red-cell count was 4,120,000 and the hemoglobin 11 mg. The white-cell count was 6900. The sedimentation rate was 85 mm. A Wassermann test was strongly positive, a Kahn test moderately positive, and an Eagle test slightly positive. The blood-sugar content was 85 mg. per 100 cc., the urea nitrogen 9 mg. and the van den Bergh 0.2 mg. (indirect).

X-ray examination of the spine was reported as follows: "There has been further bone destruction of the coccyx, and the lower segment of the sacrum shows demineralization, especially on the left. It is probably due to an osteomyelitis with bone necrosis."

Operation was performed by one of us (H.E.B.) on January 19, 1939, under spinal analgesia, employing 60 mg. of Spinoecaine in the fourth lumbar interspace. The fistulous openings were explored and found to have no communication with the rectum or anus, but to extend directly to the bone. With the probe in situ against the bone, an elliptical incision was made with the endotherm needle encircling the probe and all tissue down to the coccyx. The prevertebral pelvic fascia was freed from the coccyx, exposing the retrorectal space, and the coccyx was removed. The lower sacral segment was trimmed with a rongeur, and the roughened surface curetted. A small sinus on the right side of the anus was excised, curetted and drained, after which the entire cavity was packed loosely with iodoform gauze for 24 hours. The wound was dressed daily for 3 weeks, and graduated doses of ultra-violet light were administered. By March 15 the wound had filled in completely and was almost epithelialized, there being an area about 7 cm. long and 2 cm. wide. The patient had gained 14 pounds in weight at this time, and his general condition was greatly improved.

The pathological report of the tissue removed stated:

In the soft tissue there is a fistula lined with granulation tissue. Most of the extensive cellular exudate is such as one sees in an ordinary purulent infection, but in this case it is due to a mixed infection, for a few tubercles exist, and in one of these tubercle bacilli are present. The bone trabeculae are necrotic. The marrow spaces contain much blood, marrow cells and many polymorphonuclear leukocytes. Diagnosis: tuberculous lesion with secondary mixed infection.

According to the literature, osteomyelitis of the coccyx or sacrum, or both, is a very rare condition. Considerable time has been spent in investigating its occurrence. In 1859, Simpson⁸ in a series of lectures on injuries and diseases of the coccyx omitted any discussion of osteomyelitis. Gant⁹ cites 4 cases of necrosis of the coccyx with fistula formation, one of which he called anal fistula. He attributed necrosis of the coccyx to trauma, tuberculosis, syphilis or cancer. Yeomans¹ presents trauma as a factor in 80 per cent of his cases of coccygodynia, but none of

these cases showed bone necrosis. Monnier⁷ in 1904 reported a case of acute osteomyelitis of the coccyx in a seventeen-year-old girl who presented symptoms at first diagnosed as typhoid fever, while Boland⁸ in 1927 described a case of osteitis of the coccyx in which a stricture of the rectum had resulted and was followed by typical formation of a rectal fistula. Blount⁹ in 1928 reported a case of chronic osteomyelitis due to *Staphylococcus albus*.

On the subject of tuberculosis of the coccyx very little more has been written. The first available elaboration of the condition specifically in the coccyx was written by Lannelongue¹⁰ in 1888, who at that time pointed out the simulation of the disease to primary anorectal disease in its late stages. The first case reported was presented by Pettit¹¹ in 1790, while the first operation for the condition is credited to Mott¹² of Mobile, Alabama, in 1844. Makins¹³ reported a case in 1888 in which the patient presented symptoms of rectal obstruction and extensive ulceration of the entire perineum. Darrah¹⁴ in 1893 reported 3 cases, all of which had been admitted to his service at the Massachusetts General Hospital as ischiorectal abscesses and fistulas. David² in 1924 reported 2 cases and reviewed the literature very thoroughly, being able to find 25 other cases, including those of Darrah.

In its etiology osteomyelitis of the coccyx is no different from osteomyelitis of other bones. The commonest organism is *Staphylococcus aureus*, then *S. albus*, and finally *Mycobacterium tuberculosis*. The pyogenic forms are usually hematogenous in origin, although they have been reported as secondary to other localized infections and also to direct trauma or penetrating wounds. The tuberculous form is always secondary to other tuberculous foci and the infection is hematogenously borne.

Regarding trauma as an etiologic factor, various writers have mentioned injury as a possible exciting factor, though most patients seem to have recognized few symptoms until some time after the trauma. In the 27 tuberculous cases reported up to 1924 there was a history of trauma in 10, dating from three months to six years previous to the onset of symptoms. Our patient with tuberculous infection gave a history of an injury seventeen years previous to the presenting symptoms.

As to the incidence of the disease under discussion, statistics are at a premium. Gant's⁶ cases were equally divided according to sex and the age range was from twenty-four to forty. Monnier's⁷ patient was seventeen years old and a girl. The

cases reported by Boland⁸ and Blount⁹ were both in men, aged thirty-two and thirty-five. An analysis of the tuberculous infections reported shows 18 males and 10 females, with ages ranging from two and a half years to seventy. Trauma is reported in 11 of the cases and an associated tuberculosis in all.

Pathologically the disease varies with the acuity of the infection and the invading organism. The process begins as a localized infection of the body of the vertebra, then abscess formation and resulting bone caries and necrosis, either fulminating, as in the acute pyogenic type, or insidious, as in the tuberculous variety. The direction of the necrosis has much to do with the eventual localization of the resulting tissue involvement. If the necrosis extends anteriorly, there is a rupture through the periosteum into the retrorectal space, giving rise to signs and symptoms of rectal obstruction varying with the extent of growth of the abscess. This may burrow up or down or even perforate into the rectum. If the necrosis is sufficiently caudad in its beginning, burrowing takes place beneath the subcutaneous tissues immediately adjacent to the anococcygeal raphe, to extend into one or both ischiorectal fossae and to present the typical picture of an abscess in this region. If the necrosis directs itself dorsally, this same condition may ensue, or the abscess thus formed may perforate the skin immediately overlying the infected vertebra and present the appearance of an infected pilonidal cyst. The microscopic picture is the same as with similar lesions elsewhere in the body.

The symptoms of osteomyelitis of the coccyx may be acute or chronic, as in osteomyelitis of other bones. The acute symptoms were at first attributed to typhoid fever in 2 reported cases. The chronic form is insidious in its onset, and is early characterized by backache. All writers emphasize this as the initial symptom, which may be the only one present for a time. Lannelongue¹⁰ believes that this stage simulates *neuralgie sacro-coccygienne ou coccydienne*, which is most common in neurotic or hysterical women. David² emphasizes the presence of pain as an important symptom, causing difficulty of locomotion, inability to rise from the sitting position and absence of pain during defecation. Later, and usually after several operations, symptoms and signs develop which cannot be correctly interpreted without a careful history-taking and a thorough examination.

It is rarely before the appearance of these signs that the chronic forms of osteomyelitis of the coccyx are diagnosed. The history may or may not elicit trauma as the initial factor, although this usually antedates the onset of symptoms from

months to years. Pain over a period of several weeks or months is described as being dull in character and aggravated by motion, but without relation to the act of defecation. If seen before fistulas have developed, either spontaneously or as a result of insufficient surgery, examination will reveal either the presence of a localized abscess over the coccyx, a unilateral or bilateral abscess of the ischioanal fossae or even a retrorectal abscess. These are of the "cold" type in the tuberculous form of infection. Bimanual examination of the coccyx either before or after the development of abscess will reveal tenderness of the coccyx, and if the disease has progressed far enough there may even be crepitus of the segments due to the presence of bony fragments resulting from the necrosis. If fistulas have already developed, these are usually draining intermittently. The drainage will vary from purulent material such as that found in staphylococcal infections to the clear, watery or serosanguineous fluid associated with tuberculosis. By proper staining methods¹² the underlying organism may be detected, although usually at this stage of the disease secondary invaders are present. A roentgenogram is of great value and should be taken in every case of persisting sacrococcygeal backache and coccygodynia.

Stafford¹⁶ in 1832 admitted that he had seen an abscess connected with diseased vertebrae show itself in the loins, and in one or two cases in the nates. Autopsy of the case reported by Makins¹³ showed the primary seat of the abscess to be in the fifth lumbar vertebra. Boyd¹⁷ remarks that, though rare, pus from a psoas abscess may pass into the pelvis and form an ischioanal or even a gluteal abscess. Yeomans¹ and others have referred to the pointing of an appendiceal abscess in the perineum. Magnusson,¹⁸ writing from Borås, Sweden, reports several cases of osteomyelitis of the ischium with abscesses and fistulas in the gluteal region. He brings into his differential diagnosis the syndrome of sciatica, which must be considered before the clinical symptoms have developed sufficiently to make a diagnosis.

As to the treatment, there seems to be unanimity of opinion. The acute form requires early drainage if extensive bone destruction is to be avoided. Unfortunately, however, the diagnosis is rarely made early enough to allow only this procedure, so that, along with the chronic form, the proper treatment is ample drainage of the

area including the sinuses, with complete removal of the infected bone. All loose sequestrums should be removed and necrotic vertebrae excised, and any adjacent vertebral surfaces which show infection superficially should be curetted. The wounds should be left open and allowed to fill in from the bottom with granulation tissue. In all forms except the tuberculous, early institution of hot sitz baths are of great value in promoting healing. In the tuberculous form, localized ultra-violet therapy in increasing doses up to skin tolerance is beneficial as a local tissue stimulant. Any complicating rectal disease such as stricture, rectal fistula or incontinence due to tissue destruction may be cared for after complete healing of the coccygeal wound. Ordinarily, this requires from two to fourteen months, according to the type of infection.

SUMMARY

Two cases of sacrococcygeal osteomyelitis simulating anorectal fistulas have been reported. Even though of rare occurrence, the condition is of the utmost importance in that by careful examination a correct diagnosis may be made, with the avoidance of unnecessary multiple operations and chronic invalidism.

1527 W. Girard Avenue

REFERENCES

- 1 Yeomans, F. C. *Proctology A treatise on the malformations, injuries and diseases of the rectum, anus and pelvic colon*. Second edition 661 pp. New York: D. Appleton Century Co., 1936. Pp. 190, 208 and 248.
- 2 David, V. C. Tuberculosis of the os coccygis. *J. A. M. A.* 82:21, 24, 1924.
- 3 Kurcz, A. D. Tuberculosis of the coccyx. *Peters' Cyclopaedia of Medicine*. Vol. XI 1111 pp. Philadelphia: F. A. Davis Co., 1934. P. 433.
- 4 Lockhart Mummery, J. P. *Diseases of the Rectum and Colon*. Second edition 594 pp. Baltimore: William Wood & Co., 1934. P. 226.
- 5 Simpson, J. V. On coccygodynia and the diseases and deformities of the coccyx. *M. Times & Gaz.* 2:17, 1859.
- 6 Gant, S. G. *Diseases of the Rectum and Anus*. Third edition 697 pp. Philadelphia: F. A. Davis Co., 1905.
- 7 Monnier, L. Osteomyélite du coccyx. *Rev. d'orthop.* 5 (Series 2) 161-163, 1904.
- 8 Boland, F. K. Osteitis of the coccyx. *J. A. M. A.* 88:1833, 1927.
- 9 Blount, W. P. Osteomyelitis of the coccyx. *J. A. M. A.* 91:727, 1928.
- 10 Lannelongue, O. *Tuberculoir vertébrale* 418 pp. Paris: Asselin & Houzeau 1888. P. 355.
- 11 Pettit, J. I. cited by David.²
- 12 Mott, J. C. cited by Darrach.¹⁴
- 13 Makins, G. H. Caries of the fifth lumbar vertebra leading to chronic rectal obstruction with extensive destructive ulceration in the perineum. *Lancet* 1:876 1888.
- 14 Darrach, R. F. A report of three cases of caries of the coccyx. *Boston M. & S. J.* 128:36-38 1893.
- 15 Bacon, H. F. *Anus Rectum and Sigmoid Colon Diagnosis and treatment* 855 pp. Philadelphia: J. B. Lippincott Co., 1939. P. 293.
- 16 Stafford, R. A. cited by Smith, N. *Spinal Caries*. Second edition 146 pp. London: Smith Elder & Co., 1897. P. 76.
- 17 Boyd, W. *Surgical Pathology*. Third edition 834 pp. Philadelphia: W. B. Saunders Co., 1936. P. 706.
- 18 Magnusson, R. Tuberculous osteitis of the ischium. *J. Bone & Joint Surg.* 20:23-34 1938.

REPORT ON MEDICAL PROGRESS

EMERGENCY TREATMENT OF FRACTURES

HENRY C. MARBLE, M.D.*

BOSTON

ONE of the recent advances in the treatment of injured persons has been the great campaign carried on by the American College of Sur-

appalling; industrial accidents continue; and the injuries following sports, particularly skiing, mount yearly.

To meet this need, hospitals have established special wards for the care of the injured. These cases are now assigned to the service of surgeons with particular training in the care of traumatic cases. Once in the hospital, these patients receive proper treatment, but it is in the handling that they receive *before* arrival at the hospital that education and training are most needed.

To quote from *An Outline of the Treatment of Fractures*¹:

A man is struck by an automobile, thus breaking his leg. Except for the broken bone, without displacement, the original injury may be merely a slight periosteal tear and a mild contusion of the soft parts, but he is helped to his feet and the leg gives way and the fragments slide by each other, thus stripping off the periosteum and tearing the muscles. He falls to the

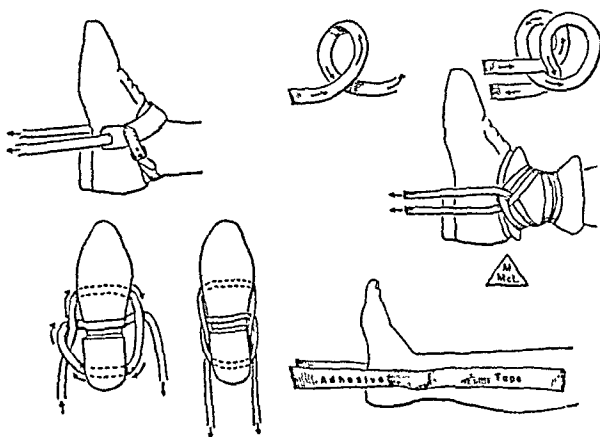


FIGURE 1.

geons to improve the transportation of the injured person from the point of accident to the hospital. This campaign has included the education of doctors, medical students, hospital interns, policemen, firemen, members of the American Red Cross and industrial organizations, railroad employees, civilians and Boy and Girl Scouts.

For doctors, demonstrations have been given at state and county medical meetings. Regional fracture committees of the American College of Surgeons have been organized. These plan to include one physician from the staff of every New England hospital. Aided by the Red Cross, members of police departments and industrial organizations have been given careful and thorough training in splinting and transportation. Motion-picture films demonstrating these methods have been made and are available. Splints in proper containers that occupy the minimum carrying space may be obtained at surgical supply houses.

During World War I, the necessity of early splinting was recognized. The same need now exists not only in military but in civilian life. Serious accidents seem to be increasing. The toll from automobile and motorcycle accidents is

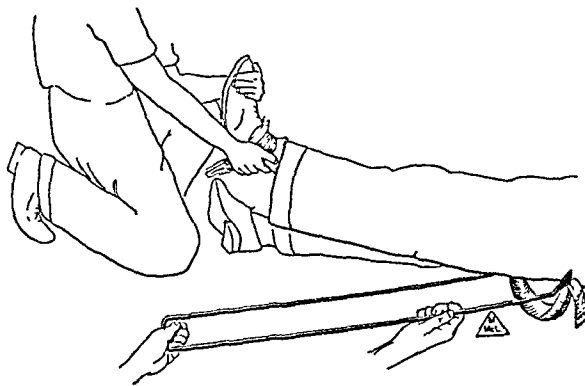


FIGURE 2.

ground only to be picked up and carried to the sidewalk with the leg dangling. Larger blood vessels are torn and the end of the bone comes through the fascia, perhaps the skin and even the trouser. He is laid at rest with a coat beneath his head and surrounded by people anxious to help. Someone sees that his leg is crooked and straightens it out. The exposed end of the bone re-enters the wound with a bit of trouser and the dirt of the street. He is lifted up and carried to a car or ambulance. This time someone carries the injured leg with better intentions than co-ordination and the ends of the bone are churned around in their bed of lacerated tissues and the contaminating organisms are well disseminated throughout the area. During his ride and in the transfer to the accident ward

*Assistant in surgery, Harvard Medical School; assistant visiting surgeon, Massachusetts General Hospital.

or the doctor's office, unless he has been carefully splinted, there is more jolting and more damage. Would that his troubles were over, but too often the sad story continues. Lack of sufficient protection as he is lifted to and from the x-ray table and as he is being anesthetized results in still more injury.

Compare this exaggerated picture with a similarly injured man who is allowed to remain where he is until a proper splint can be applied, or at least until he can have someone pull hard on his foot as he is being lifted and carried, whose examination is thoroughly but gently carried out, and whose treatment is instituted with but little additional injury. The difference

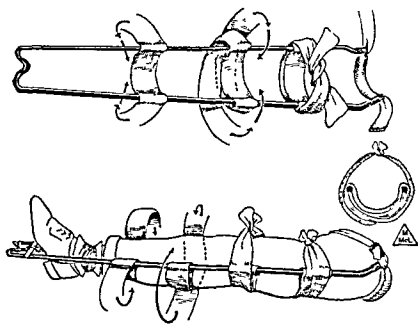


FIGURE 3.

in these two cases as regards periods of disability and amount of permanent functional disturbance is great.

All cases of accident, particularly those to the extremities, should *not* be moved until the injured part or parts have been carefully splinted. Injuries to the spine require special handling.

Transportation, depending on the circumstances, may be furnished as follows:

- Ambulances
- Police-department vehicles
- Fire-department vehicles
- Commercial vehicles
- Privately owned vehicles
- Sleds, toboggans and stretchers
- Individuals

An attempt is being made to educate and train all those who might be responsible for transportation.

The necessary splint equipment is as follows:

- Keller-Blake leg splint
- Murray-Jones arm splint
- Stretcher
- Triangular bandages (six)
- Roller bandages
- Sterile dressings and aqueous iodine
- Blanket

These are now obtainable in surgical supply houses and can be carried in a small space. When manufactured traction splints are not available, satisfactory fixed traction can be maintained by using notched boards, broomsticks, rakes, branches of trees and so forth. Methods for applying these improvised splints are described in the *American Red Cross First Aid Text-Book*.²

Some of the general rules to be followed are as follows:

A splint should always be applied if there is any suspicion of fracture.

The principles of fixed traction and immobilization are used in all splinting.

If there is a wound, paint the surrounding skin with aqueous iodine and apply a sterile dressing.

The splint should be applied where the person falls, *before* moving.

INJURIES TO THE HIP AND LEG

A leg splint (Keller-Blake) should be applied. The procedure is as follows:

Cover the patient with a blanket.

Have a helper steady the leg just above the

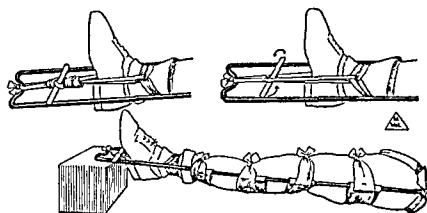


FIGURE 4.

ankle with a firm grip to prevent motion while applying an ankle hitch (Fig. 1):

With bandages and two clove hitches, one on the inner side and one on the outer side

With bandage sling to outside of shoe

With special strap (Army) or laced device about the ankle

With adhesive tape.

Place a firm pull with both hands on the foot and ankle, keeping this up until the splint is fully applied.

Still pulling, raise the injured limb a few inches.

Slide a half-ring splint under the thigh from

the outside, fitting it at the top of the thigh, with the rods lateral (Fig. 2); buckle the groin strap.

Hammock the leg in the splint with four or five cravat bandage or towel slings (Fig. 3).

Tie the extended ends of the ankle-traction

With bandages and two clove hitches, one in front and one in back

With a triangular-sling hand hitch (Red Cross)

With adhesive tape

Place a firm pull with both hands on the

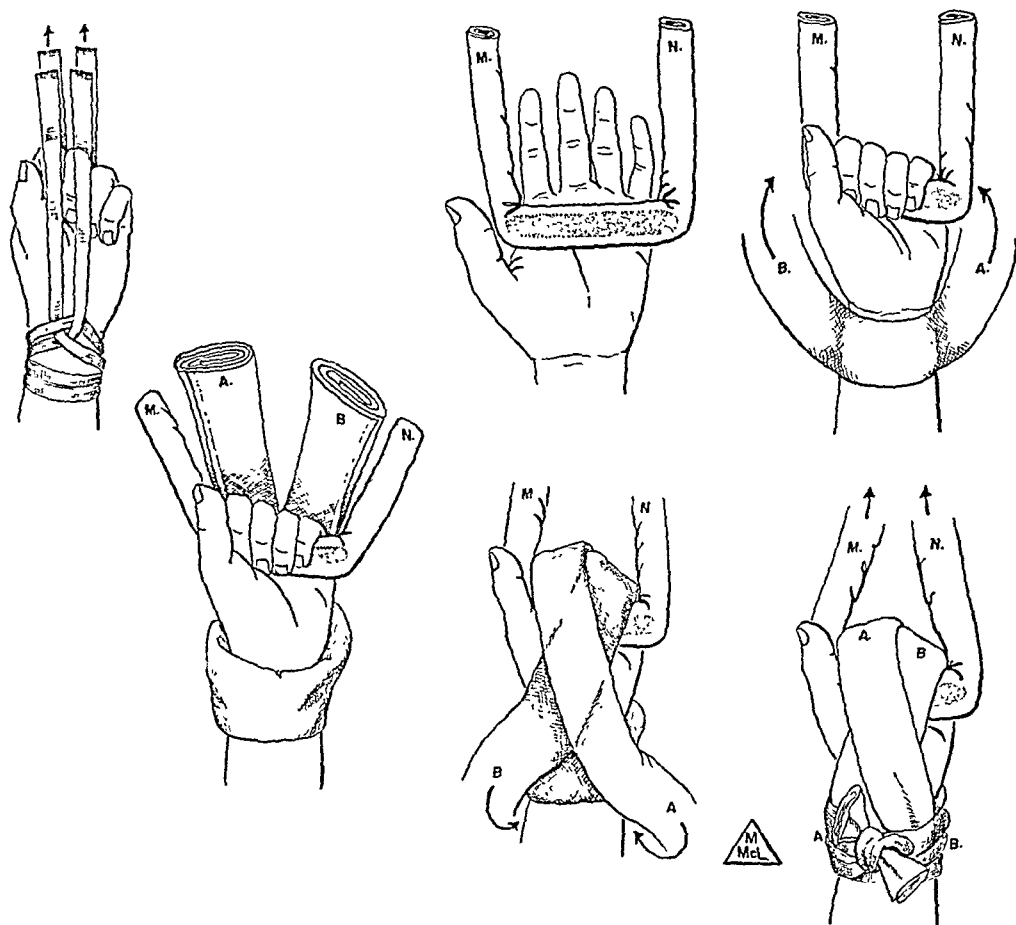


FIGURE 5.

hitch over the end of the splint; insert a stick between the ends of the hitch and twist until firm traction is established (Fig. 4).

On a block, elevate the lower end of the splint 6 inches.

INJURIES TO THE ANKLE AND FOOT

A folded blanket or pillow reinforced laterally by thin splint boards all bandaged firmly in place furnishes satisfactory immobilization.

INJURIES TO THE SHOULDER AND ARM

An arm splint (Murray-Jones) should be applied. The procedure is as follows:

Cover the patient with a blanket.

Have a helper steady the arm just above the wrist with a firm grip to prevent motion while applying a wrist hitch (Fig. 5):

wrist, keeping this up until the splint is fully applied.

Thread on the arm splint.

Tie the extended ends of the wrist-traction hitch over the ends of the splint; tighten with a windlass consisting of a stick or nail (Fig. 6).

Hammock the arm in the splint with cravat or bandage slings.

INJURIES TO THE WRIST AND HAND

A folded blanket or a well-padded splint board, extending from the elbow to the finger tips and firmly bandaged, plus a sling, furnishes adequate fixation.

INJURIES TO THE BACK

To transport a person with an injury to the spine, a rigid litter or stretcher is necessary. This may consist of the following:

- A firm stretcher
- A wide plank
- A door
- A toboggan

A blanket should be used for covering

If the injury is below the shoulders, the patient is usually most comfortable face down, with the head pillowed by the arm (Fig. 7). The injured person should be rolled onto the litter using many

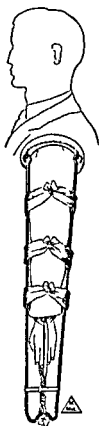


FIGURE 6

hands and avoiding at all costs even momentary flexion of the spine.

If the injury is above the shoulder, the head



FIGURE 7.

should be steadied by light traction, which can be applied by cupping the head and chin with

both hands from above and gently pulling in the line of the body. The patient should be rolled onto the litter face up, in this case avoiding flexion or extension. Steady traction to the head should be maintained during the entire period of transportation (Fig. 8).

If the patient is found lying unconscious, particularly if he shows bruises about the head or face, it is wiser to assume the worst injury—a broken neck—and transport him accordingly.

* * *

Transportation often becomes the duty of civil-

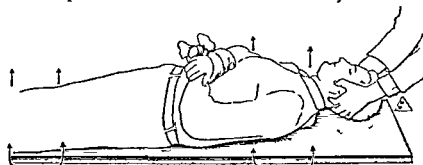


FIGURE 8

ians. If carried out carefully and thoroughly, the patient will arrive at the hospital in the best possible condition. There is less shock, the pain is less, the broken bones have not overridden, and the healing process is given the chance to proceed normally. Irreparable harm is often done in moving the patient incorrectly from the scene of the accident to the hospital. Immeasurable good is done by proper handling.

Every physician who is not thoroughly familiar with these modern concepts concerning the emergency treatment of fractures should learn them. Some doctors carry traction splints in their cars at all times. All doctors' cars and all ambulances should be so equipped, and the drivers properly trained to use the equipment.

270 Commonwealth Avenue

REFERENCES

- 1 Committee on the Treatment of Fractures. *An Outline of the Treatment of Fractures*. Second edition. 40 pp. Chicago: American College of Surgeons, 1933. P. 7.
- 2 *American Red Cross First Aid Text Book*. 248 pp. Philadelphia: P. Blakiston's Son & Co., 1937.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 26431

PRESENTATION OF CASE

A seventy-three-year-old retired silversmith entered the hospital complaining of tenderness in the right lower quadrant of the abdomen of two weeks' duration.

Four years before admission the patient entered the hospital with the classic signs and symptoms of an enlarged prostate. A perineal prostatectomy and bilateral vasectomy were performed, and he was discharged in three weeks, having had an uneventful convalescence. The pathological report was "hyperplasia of the prostate."

During a routine examination two months before admission, pus was found in the urine, and six weeks later, tenderness in the right lower quadrant, which continued until admission.

The patient had broken his arm twice in childhood, and many years before admission he had fractured the head of the left femur, which resulted in limitation of movement of the hip joint. He had had an attack of substernal distress while cranking a car nineteen years before admission and a similar attack nine years before admission. Five years prior to entry the attacks became more frequent on exertion, and the pain sometimes radiated down both arms. His physician restricted his activity and prescribed aminophyllin three times a day and nitroglycerin tablets during attacks. The patient used only two of these during the next four years, but had taken six during the year before he was admitted.

In addition a herniorrhaphy had been performed seven years before admission, and a small cancer had been removed from the left cheek more than four years prior to entry.

Physical examination showed a well-developed and well-nourished man lying comfortably in bed. Numerous small licheniform areas were present on the chest and back. Examination of the heart and lungs was negative; the blood pressure was 130 systolic, 70 diastolic. The temporal, brachial and radial arteries were tortuous. There was tenderness in the entire right side of the abdomen, most marked in the right upper quadrant; the former point of maximum tenderness, indicated by the

patient in the right lower quadrant, was not demonstrable at the time of examination. There was a hard, nodular, tender mass immediately to the right of the umbilicus. The left femur was 5 cm. shorter than the right, and the left trochanter was more prominent than the right. There was a slight compensatory scoliosis.

The temperature, pulse and respirations were normal.

Examination of the urine showed a + test for albumin, with 100 white blood cells per high-power field and many bacteria. Examination of the blood showed a red-cell count of 4,400,000 with a hemoglobin of 14.8 gm. (photoelectric-cell technic), and a white-cell count of 7900 with 69 per cent polymorphonuclears. The blood sugar was 79 mg. per 100 cc., and the nonprotein nitrogen of the blood serum 32 mg. A blood Hinton test was negative. A phenolsulfonephthalein test showed 5 per cent output of the dye the first fifteen minutes, and 55 per cent in one hour.

X-ray examination after a barium enema showed the tip of the cecum to be blunt, with a concave defect corresponding to the palpable mass. The barium given by mouth passed into the small bowel readily. The defect in the cecum reached the ileocecal valve but did not obstruct the lumen. One of the films revealed a pressure defect on the ileum about 3 cm. medial to the tip of the cecum, and on this film there was a suggestion that most of the mass was outside the cecum.

An electrocardiographic recording showed a normal rhythm and a rate of 65, with slight widening of the S waves in all leads and a slightly long PR interval—0.20 second.

On the fifth hospital day the patient complained of a sudden severe pain that was dull in character and sharply localized over the xiphoid. The attack lasted for five minutes and then passed away completely. There were no accompanying symptoms, and a physical examination ten minutes later revealed no change in his condition. Two days later an exploratory laparotomy was performed.

DIFFERENTIAL DIAGNOSIS

DR. ARTHUR W. ALLEN: We have an elderly man who was admitted to the hospital with a mass in the right side of the abdomen that probably was of short duration. I say "probably," because he was in some department of the hospital two months prior to this entry, at which time they found pus in his urine but made no note of any mass in his abdomen. If it had been the same size and consistence that it was when the patient was admitted, they would doubtless have noticed it.

One should not worry too much about pus in the urine in a man of that age who had had a prostatectomy. I believe that this present illness does not have any bearing on the prostate operation or that it has anything to do with the urinary tract. The tenderness found in the right lower quadrant two weeks prior to entry is important. The record does not say whether the mass had increased in size between the time that tenderness was first noted and the time the patient was admitted to the hospital, but apparently in that two-week interval the location of the tenderness had changed from the right lower to the right upper quadrant. This complicates the picture.

I am not sure from the electrocardiographic tracings, whether the patient had coronary disease, but he had a history that would indicate such a disease; we know he had arteriosclerosis. Whether either of these conditions had any bearing on this picture, is very doubtful. I do not believe that this tender, palpable mass was an aneurysm. There is no evidence of its being expansile, and it came up rather too rapidly.

In a man of this age with a palpable mass in the abdomen, one invariably thinks first of cancer, and in this case it is a distinct possibility. A patient may have carcinoma of the cecum, with a large mass and subacute perforation, that has not been foreshadowed by any symptoms. It might reach this stage without giving us any more information than we have in this case. On the other hand, it is fairly unlikely. We should not expect a patient to be in such a perfect state of nutrition; furthermore, there is no mention in the hospital record of disturbances of the gastrointestinal tract so far as appetite is concerned, or any mention of change in bowel habits. Also opposed to the diagnosis of cancer is the fact that there was no anemia. I do not mean to imply that carcinoma of the cecum or ascending colon cannot be present with a very large mass without anemia. Although anemia is frequently present, it is not necessarily so.

A confusing feature in trying to interpret this as an inflammatory mass is the fact that the patient had an absolutely normal white-cell count, with a normal differential. This further complicates the picture.

DR. JAMES R. LINGLEY: As you see on these films, the barium enema reaches this point opposite the ileocecal valve, where it meets an obstruction. The tip of the cecum is not filled on any of the films, and no barium enters the terminal ileum. On this film, taken six hours after the motor meal, the terminal ileum is well filled, there is filling of the ascending colon, and the cecum

again shows the same defect. The point that I am unable to decide is whether this defect so intimately associated with the tip of the cecum is caused by extrinsic pressure or by an intrinsic mass.

DR. ALLEN: Can you see the kidney in the right side in any of these films?

DR. LINGLEY: The kidney is pretty well obscured by the hepatic flexure, but I think it is in normal position and of normal shape.

DR. ALLEN: Because of the patient's excellent condition, the lack of anemia and the lack of gastrointestinal-tract symptoms, I am going to hazard the guess that this is a subacute inflammatory process originating in the appendix, and that we are dealing with a subacute appendiceal abscess. I am making this diagnosis in the face of the normal white-cell count, which might have been highly elevated at some previous time in the earlier part of the illness. We have had four or five similar cases in which a mass in this region in elderly people has been interpreted as cancer and operated on under that diagnosis, the final diagnosis being that of an inflammatory process based on appendicitis. My second choice is cancer with subacute perforation, the lesion arising in the bowel in spite of the fact that the x-ray interpretation indicates that this was an extraluminal lesion. There are many other unusual situations that might explain this picture—mesenteric adenitis with a large mass outside of the bowel, or tuberculous lesion in the neighborhood of the ileocecal valve. We always must consider the possibility of lymphoma when dealing with any tender abdominal mass. These are possibilities that one ought to mention and consider, but my first choice is an inflammatory mass of appendiceal origin, and my second, cancer of the colon, with secondary inflammation around it.

DR. LELAND S. MCKINTUCK: There was one point in the history which is a little different from that presented here, possibly because the patient did not know it—a mass was found by the urologist. The patient complained of a little soreness in his side, and a mass was felt at that time. That was what started the investigation that later led to his coming into the hospital and being examined. The X-ray Department said "probable carcinoma of the cecum." Operation was done with the diagnosis uncertain. We did not know whether he had carcinoma with a subacute process around it or a low-grade appendiceal abscess. One could not be sure of the best way to attack the problem. We elected to approach it as though it were a carcinoma. At operation the tumor mass was palpated with the greatest care, but no diag-

nosis could be made. The liver was free from metastases. I thought that the mass, as I felt it from within the abdomen, was probably malignant. He had an ileotransverse colostomy done as the first step of a two-stage direct approach to the tumor mass at a later time.

DR. TRACY B. MALLORY: I take it that the subsequent course was never good enough to make any further operation possible?

DR. MCKITTRICK: No; the subsequent course was such that the second "operation" was done by Dr. Mallory. The patient's immediate response to operation was perfectly satisfactory. However, he then ran an unexplained fever. We were confident that he did not have peritonitis. On the other hand he had more tenderness in the right flank than he had had previously, but even that did not wholly satisfy the clinical picture which he presented. He developed cerebral symptoms and died, I have forgotten how many days after operation; it was a death that we could not satisfactorily explain. We did think that there had been extension of the infection in the right flank. We could not quite see how that was responsible for the course that he ran, but we believed that he did not have general peritonitis. The ileotransverse colostomy was functioning satisfactorily.

PREOPERATIVE DIAGNOSIS

Carcinoma of the cecum.

DR. ALLEN'S DIAGNOSIS

Subacute appendicitis, with abscess formation?

Carcinoma of the colon, with subacute perforation?

ANATOMICAL DIAGNOSES

Appendiceal abscess.

Brain abscess, right frontal area.

Pulmonary congestion and edema.

Cholecystitis, chronic.

Cholelithiasis.

Cholesterosis of gall bladder.

Cardiac hypertrophy, hypertensive type.

Operative wound: left rectus incision for ileotransverse colostomy.

Arteriosclerosis, coronary and aortic.

Hydrothorax, bilateral.

PATHOLOGICAL DISCUSSION

DR. MALLORY: At autopsy 700 cc. of slightly turbid fluid was found in the peritoneal cavity; there was a very large firm mass that was evidently mostly omentum. On breaking into it, a central abscess cavity containing 60 cc. of pus was found, and in its midst was the stump of the

appendix. The actual cause of death, however, was not the peritoneal sepsis. It was a metastatic abscess of considerable size in the right frontal lobe of the brain. There was evidence of chronic cholecystitis, and a few small stones were present in the gall bladder, but there was no evidence that this infection played any part in the fatal outcome. The coronary arteries showed only slight atheroma, and there were no scars of myocardial infarction. There was, however, moderate hypertrophy of the hypertensive type.

DR. ALLEN: I think that the proper operation was done for this particular patient. If you break into such a mass thinking it is an appendiceal abscess and find it to be carcinoma, you have robbed the patient of some of his chances of having a successful extirpation of the tumor. I think one might well argue that had the abscess been drained at the first operation he might have been spared the metastatic abscess later on, but this does not necessarily follow. He could have had a brain abscess after drainage of the appendiceal abscess. I am sure that if I had had this problem I should have handled it exactly as Dr. McKittrick did, that is, with a two-stage operation.

DR. MCKITTRICK: Dr. Allen has suggested the difficulty, at operation, of differentiating cancer of the cecum and an appendiceal abscess. It is of interest in this connection that after the pathologist had removed the abdominal contents and arranged them on the table, he made a diagnosis of cancer. Not until he had broken through the abscess and into the cecum could he be sure there was no cancer.

CASE 26432

PRESENTATION OF CASE

A sixty-three-year-old woman entered the hospital complaining of difficulty in breathing of five weeks' duration.

The patient stated that at the age of twenty-eight she had been a victim of a milk-borne streptococcal infection in which all her joints became red and swollen, and that during this time an aortic valvular lesion was discovered. She lived a normal active life until one year before admission, when she began to suffer from breathlessness, anorexia and loss of weight. The dyspnea was marked at the beginning of this period, but improved and did not return in all its severity until five weeks before admission, although she had had occasional attacks of nocturnal dyspnea. In addition she had noticed swelling of her ankles. Two days before admission the patient developed an unproductive cough and hoarseness.

The past illnesses and family history were irrelevant.

Physical examination showed a well-developed but poorly nourished woman, who appeared chronically ill and lay propped up in bed breathing quietly. The neck veins were distended to about 5 cm. above the sternum. The heart was moderately enlarged to the left, and a systolic thrill was palpable at the base. A harsh systolic murmur was heard in the aortic area, with a diminished aortic second sound; the sounds were of poor quality, with a gallop rhythm. The blood pressure was 120 systolic, 75 diastolic. At the lung bases the percussion note was dull, the tactile fremitus and breath sounds were diminished and a few moist rales were heard. There was pitting edema of the legs to the knees.

The temperature and respirations were normal, and the pulse varied between 80 and 120.

Examination of the urine showed a + test for albumin, with 30 white blood cells per high-power field, and many unidentified bacteria. The blood showed a red-cell count of 4,760,000 with a hemoglobin of 11.5 gm. (photoelectric-cell technic), and a white-cell count of 12,100. The nonprotein nitrogen of the blood was 42 mg. per 100 cc. A blood Hinton test was negative.

Four days after admission the patient complained of severe "gas pains" in the right upper quadrant that radiated to the back to a point immediately below the scapula. Examination at that time revealed an enlarged very tender liver. In general the patient's course was progressively downhill, although treatment improved the peripheral edema. In the last few days of her illness she became disorientated and developed a decubitus ulcer of the sacrum. The patient died two months after admission.

DIFFERENTIAL DIAGNOSIS

DR. EDWARD F. BLAND: This is a fairly clear-cut story, and the physical signs are well described in so far as the structural lesion is concerned. Perhaps we should consider this aspect of the case before discussing the question of etiology. It seems reasonably clear that there was aortic stenosis of considerable degree. All the physical signs are consistent with that diagnosis, namely, a harsh, basal systolic murmur maximal to the right of the sternum and accompanied by a systolic thrill and by diminution in the intensity of the second sound. To make the picture complete we might like a narrow pulse pressure, but we need not be disturbed by its absence, since some patients with well-marked aortic stenosis may even have hypertension. About half the patients with aortic

stenosis also have a very slight degree of aortic regurgitation, manifested by a faint diastolic murmur along the left border of the sternum. It seems remarkable that all of them do not have a slight degree of aortic regurgitation. A fair number of patients with well-marked aortic stenosis also have evidence of other valvular disease, especially of the mitral valve, but from this record we have no indication of such disease. Finally, the clinical course that this patient ran is characteristic of well-marked aortic stenosis, possibly calcific in type.

Next we must consider the etiology. I hesitate somewhat to reopen that question again. The cause of this lesion has been the source of much discussion and considerable disagreement among capable observers. I think most people agree that aortic stenosis is superimposed either on previous inflammatory lesions in the valve cusps or in that vicinity, or less often on a congenital defect, usually a bicuspid aortic valve. The latter, of course, is relatively rare. There has been a tendency among pathologists to relinquish previously held ideas concerning the possible role of Mönckeberg's sclerosis in some of the otherwise unexplained cases. Finally, as regards etiology, a few years ago it was suggested that in an occasional case of well-marked aortic stenosis, the preceding inflammatory change in the valve might perhaps have been due to a mild subacute bacterial endocarditis from which the patient was fortunate enough to recover. There is not really much evidence to favor this point of view. From the clinical standpoint a history of rheumatic fever or chorea is obtained in one third to one half of this group of patients. In a considerable additional number, bringing the total up to about 75 per cent, there is a past history of unusually frequent sore throats and respiratory infections. From the pathological point of view, I am of the opinion that Dr. Louis Gross before he died was inclined to think that the majority represented superimposed calcification on old rheumatic damage of the valve. At a meeting last year in Pittsburgh, Dr. Ernest Hall suggested that perhaps all or at least a very high percentage were of this origin. The belief in the pathology department of this hospital is that a considerable number, perhaps not all, are the result of healed rheumatic inflammation in the valve.

The incidence of this condition is of some interest. In this hospital it is noted about twice in a hundred postmortem examinations, and as one sees cardiovascular patients, about three in a hundred have physical signs of this lesion. It is also true that it is commoner in the northern states than in the South, where infections in general, and rheumatic

infection in particular, are somewhat less common.

The clinical features have been well described by numerous observers, and this patient's course is fairly characteristic. The valve lesion is usually well tolerated for many years, but when cardiac failure finally ensues, the heart fails to respond satisfactorily to digitalis and diuretics. We are not told much about the therapy of this case, but we can assume that the patient had received rest, digitalis and diuretics. The course, however, was progressively downhill, as we should expect. It is also true that many of these patients have angina pectoris, but I could identify nothing in this record as angina pectoris. Many of these patients have spells of dizziness and faintness, and sudden death is not uncommon with well-marked aortic stenosis. Relatively few develop subacute bacterial endocarditis. Auricular fibrillation, which I assume was not present in this case, is relatively rare except in those patients in whom aortic stenosis is associated with rheumatic disease of the mitral valve.

There are two questions we might like to raise, but I do not know whether the information would be particularly helpful. First, nothing is said about this patient's electrocardiogram. We should expect that, if characteristic, it would show some degree of left-axis deviation. Intraventricular block is not so uncommon as auriculoventricular block. Abnormal T waves are almost the rule. Finally I am curious to know what the x-ray examination revealed in this patient, because in our experience here approximately 75 to 80 per cent have calcium deposits superimposed on the valvular lesion. The more interested we have become in this condition, the oftener we have been able to detect the calcium under the fluoroscope. It is more easily shown under the fluoroscope than in films, even with films taken with a special technic to demonstrate it. Another point in relation to the x-ray findings that might be of interest is the contour of the left auricle. Although there were no physical signs suggesting involvement of the mitral valve, it would have been interesting to confirm this by careful study of the left auricle under the fluoroscope.

One is left, then, with not much choice as to diagnosis. One other condition might be mentioned in passing. I know of three or four younger people with congenital subaortic stenosis who are in good health. I suppose some time or other we may see this condition in an older person, since it causes relatively little strain on the heart. I suspect that this was not the answer here. I

will make a diagnosis of aortic stenosis, probably calcific, with congestive heart failure.

DR. HOWARD B. SPRAGUE: I can answer a few of the questions that Dr. Bland asks. I saw this woman first in January, 1939, when she began to have attacks of cardiac asthma, but her previous story included a year of very definite angina pectoris on exertion and a burning sensation under the sternum that was relieved by rest. The cardiac asthma started abruptly and disturbed her every night. At that time she showed evidence of aortic stenosis and an aortic diastolic murmur. The blood pressure when she was first seen was 180 systolic, 105 diastolic. There were a few rales at the lung bases and some sacral edema. She was digitalized at that time, with complete relief of the symptoms for several months. In fact, I did not see her again for over a year, and then she gave a story of having had only three attacks in the intervening period; she had, however, been very much limited in activity on account of dyspnea and substernal oppression. She had become very depressed because she had had to change abruptly from being a very active woman to one who was partly bedridden. She then showed pulsus alternans and increasing congestive failure, and was admitted to the hospital for mercurial therapy. I should add that after I saw her at home she came to the office, where definite calcific aortic stenosis, without evidence of mitral disease, could be demonstrated under the fluoroscope.

DR. BLAND: In view of the history of angina pectoris mentioned by Dr. Sprague, may I ask him if he expects to find the coronary arteries in good or poor condition?

DR. SPRAGUE: It would not be fair for me to answer that, since I know what the autopsy showed.

DR. PAUL D. WHITE: I saw the patient with Dr. Sprague and thought that she had a very high degree of aortic stenosis; it is surprising that she lived as long as she did with the signs that showed on physical examination.

CLINICAL DIAGNOSES

Rheumatic heart disease, old.
Calcific aortic stenosis.
Decubitus ulcer.

DR. BLAND'S DIAGNOSES

Aortic stenosis, probably calcific.
Congestive heart failure.

ANATOMICAL DIAGNOSES

Aortic stenosis, calcareous.
Pulmonary infarcts, multiple, old and recent.
Thrombosis, right popliteal vein, antemortem.

Cardiac hypertrophy, hypertensive type.
Nephritis, chronic vascular.
Hydrothorax, bilateral.
Chronic passive congestion of liver, slight.
Pulmonary edema, slight.
Peripheral edema, slight.
Arteriosclerosis, coronary and aortic, slight.
Decubitus ulcer.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: The postmortem examination showed calcific aortic stenosis of a very severe grade. The valve, when one looked down on it from above, showed a slit-like opening between two cusps that were almost of equal size, although one was slightly larger than the other. Both sinuses of Valsalva were completely filled with irregular nodules of very hard calcified material. There can be no question that there was an underlying bicuspid aortic valve. In a bicuspid valve the two valves are never quite of equal size; the two fused cusps, however, measure somewhat less than the sum of two normal cusps, and the remaining cusp is always greater than any single normal cusp would be, and that was very clearly evidenced here. In many cases it is quite impossible to decide grossly whether a bicuspid valve underlies the lesion. My personal impression would be to disagree with Dr. Bland and think that very often a bicuspid valve underlies this condition. However, members of my own department do not always agree with me, and you can therefore see that it is an unsettled question. It is possible histologically to distinguish bicuspid valves with reasonable certainty by studying the

relation of the various layers of the aortic wall to each other at the point of commissure. That can easily be done when there is no calcification, but in a case like this, decalcification is so difficult and takes so long that it is ordinarily impossible to stain the wall successfully; most of our efforts have been very disappointing, and that has been the experience of almost everyone else. The coronary arteries showed moderate but not severe atheroma without narrowing. There was no thrombosis. The mitral valve was grossly normal.

A surprising finding at autopsy that was not foreshadowed, so far as I can see, by anything in the clinical story was a number of quite large pulmonary infarcts—four good-sized ones, three of which had evidently been present for a long time. One was fairly fresh and may have occurred during the stay in the hospital, and the others certainly antedated admission. It is not impossible that the final episode of failure may have followed infarction, although we have no clear evidence of that. Usually with pulmonary infarction one can count on a significant rise in temperature, but even that was absent in this case. The temperature did not go above 99.2°F. at any time in the hospital, probably because the majority of the infarcts occurred and the febrile reaction was over before the patient was admitted. As regards the etiology, Dr. Bland has already outlined the argument, and I can only say that this case is one that I can regard as exceptional because it had a clear-cut history of rheumatic fever, which very few of the cases show, and a grossly negative mitral valve.

DR. WHITE: How big was the heart?

DR. MALLORY: It weighed 650 gm.

The New England Journal of Medicine

Formerly the
Boston Medical and Surgical Journal
Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE
ON PUBLICATIONS

Official Organ of

THE MASSACHUSETTS MEDICAL SOCIETY
THE NEW HAMPSHIRE MEDICAL SOCIETY
THE VERMONT STATE MEDICAL SOCIETY

EDITORIAL BOARD

Joseph Garland, M.D.	John P. Sutherland, M.D.
William B. Breed, M.D.	Stephen Rushmore, M.D.
George R. Minot, M.D.	Henry R. Viets, M.D.
Frank H. Lahey, M.D.	Robert M. Green, M.D.
Shields Warren, M.D.	Charles C. Lund, M.D.
George L. Tobey, Jr., M.D.	John F. Fulton, M.D.
C. Guy Lane, M.D.	A. Warren Stearns, M.D.
William A. Rogers, M.D.	Dwight O'Hara, M.D.

ASSOCIATE EDITORS

Thomas H. Lanman, M.D.	Donald Munro, M.D.
Henry Jackson, Jr., M.D.	
Walter P. Bowers, M.D., EDITOR EMERITUS	
Robert N. Nye, M.D., MANAGING EDITOR	
Clara D. Davies, ASSISTANT EDITOR	

SUBSCRIPTION TERMS: \$6.00 per year in advance, postage paid, for the United States, Canada, \$7.04 per year; \$8.52 per year for all foreign countries belonging to the Postal Union.

MATERIAL for early publication should be received not later than noon on Saturday.

THE JOURNAL does not hold itself responsible for statements made by any contributor.

COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston, Massachusetts.

MEDICAL EDUCATION IN THE UNITED STATES

MEDICAL education always has been a baffling affair to many people: to students who must be educated, to teachers who must educate, and to doctors who must practice. Thus, the topic of medical education has been thrashed out all over New England since at least 1782, and there still is grave doubt in the minds of those interested in the problem as to whether there yet is any certain formula to describe the best way of managing so complex a contrivance.

In 1933 the Council on Medical Education and Hospitals of the American Medical Association voted to undertake a comprehensive re-survey of the medical schools of the United States and Canada. The final result was recently printed in the form of an extensive report.*

*Committee on Medical Education and Hospitals. *Medical Education in the United States, 1934-1939*. 249 pp. Chicago: American Medical Association, 1940.

This report is full of interesting data and is worth careful study. It has been written skillfully; instead of describing individual schools and making comparisons that might well be invidious, the book deals with broader views: the aims and policies of American medical education, differences in the programs of organization and administration in different schools and trends in medical education.

As in every comparative analysis of an imponderable substance like quality, among medical schools, too, it appears that there are many that are good, some that are better, and some that are still better. Underlying medical education in all schools, however, are two peculiarities that are worth noticing.

Medical education today is expensive,—from two to seven times more expensive than any other form of professional education,—and this is chiefly the result of its being so time-consuming. Nowadays more than half the medical students experience four or more years of college study before they begin the study of medicine. Thirteen of the schools require a year of internship after four years of medical-school training before their students may receive their degrees. Specialty practice has become popular, and adequate preparation for any of its forms appears to require intensive training for a considerable period of time after a man has been through medical school and hospital. All this may be sound, but it greatly increases the cost of medical education. The schools with greatest wealth are likely to attract the most active teachers and to offer their students the best facilities for study and inspiration. There is indeed a strong responsibility for leadership in medical research and teaching resting in the hands of those medical schools that have been fortunate enough to have obtained large endowments.

The recent popularity in specialism has tended to shift the teaching of the specialties out of the medical school. This is satisfactory to the student who can afford to acquire training in a specialty but not so helpful to the one who must set up his shingle in general practice as soon as he can. It is said that some have had teaching in the specialties so neglected in their undergraduate days

that when they were on their own they found themselves unable to make a complete examination of a patient. And this seems scarcely the best way to improve the average of ordinary work.

On the whole, however, the present health of medical education in the United States is in a vastly more vigorous state than it was in 1910 when Abraham Flexner's report appeared. Bad schools have been deleted, good schools have been strengthened, the general level of teaching has been raised, and doctors are better and more intelligently trained than they were a generation ago. Medical education is by no means perfect. But what system of education is?

ONE PROBLEM IN THE DIAGNOSIS OF CANCER

ONE of the aspects of the cancer problem that makes diagnosis difficult is the infrequency of cancer cases in relation to the general type of patient coming to the practitioner's office, as well as the tendency to a concentration of cancer cases, through one means or another, so that many practitioners see very few. In Massachusetts, a physician might expect to see two to three cancer patients a year if the cases were evenly distributed. The effect of concentration is not definitely known, but undoubtedly patients who suspect that they have cancer go to men who have established a reputation for special interest or competence in that field.

A recent paper by McDowell* of the United States Public Health Service gives the results of a study of this problem in the Pittsburgh area. On the basis of case records and death certificates, there were, in the year 1937, 6103 cases of cancer under medical care or certified as dying from cancer. Strikingly enough, over 50 per cent of these cases were reported by 0.3 per cent of the doctors and 16 per cent of the hospitals. Nearly half the doctors and half the hospitals reported no cases of cancer during this period. The need for inten-

sive cancer education in this area is shown by the fact that 59 per cent of fatal cases had been diagnosed as malignant less than six months before death, and 80 per cent of them less than a year. This means a long period of delay in the vast majority of cases.

If the experience in Massachusetts can be trusted the only way to cut down this delay period is through intensive educational effort among the laity, guided by and with the co-operation of physicians.

OBITUARY

HENRY JACKSON

1858-1940

Henry Jackson died on October 4, 1940, in his eighty-second year. So is another taken from the fast-thinning ranks of those physicians who practiced the art of medicine and at the same time helped materially to lay the solid foundations upon which our science of today is built. His life epitomized the ideal family doctor.

All who had contact with Dr. Jackson, whether patient, friend or young student of medicine, adored him. What formal teaching he did was at the Boston City Hospital in connection with the Harvard Medical School. His students and more especially his house-officers never tire, even to this day, of quoting "Uncle Henry" and never fail, whenever they get beyond their depth, to fall back on his sound common sense and never-to-be-forgotten aphorisms. Informally he taught much sound medicine to many, — usually by precept and example, — and until his retirement he was constantly searching for new roads to perfection — as witness his own early use of the McKenzie polygraph in the study of heart disease. But above all, he taught a generation of students to look on patients as human beings and to regard their diseases in the light of their personal idiosyncrasies.

He had, to be sure, his own lovable peculiarities, which only endeared him the more to his friends and patients. No one who really knew him could imagine Dr. Jackson leaving his house without his famous square-topped hat. His presence in the home was always cheerfully announced from just inside the front door no matter if the family were three stories up, and even the sick-

*McDowell, A. J.: The incidence of cancer in Pittsburgh and Allegheny County, Pennsylvania, 1937. *Pub. Health Rep.* 55:1419-1451, 1940

est patient's morale rose promptly in response. He could do anything with children of all ages, and was as fond of them as they were of him. When he was on service at the Boston City Hospital, he invariably carried a pocketful of bright new pennies and solemnly presented one to each sick child every day. A logician and purist in all things, he insisted on kindly efficiency, self-respecting industry, unvarnished truth and consideration for others in all about him, and set the example by imposing the same standards on himself. In the days when thyroid disease and so-called "sciatica" were much in the medical eye, he was just as insistent in refusing to Anglicize the French word *goitre* as he was in condemning the inadequacy of a wastebasket diagnosis such as sciatica.

He had a great sense of personal dignity and demanded and received the respect due him. In return he expected all those about him to show the same attributes, and he was the first to accord them due respect. He abhorred all sham and dishonesty under any guise. He had a sharp tongue and could, on occasion, put it to good use. He was far quicker to praise than to blame and saw to it that credit was given where credit was deserved.

After his retirement, his physical and mental activities were unabated, and he continued to find intellectual outlets for his many energies, among them the study of conversational French and French literature. During the last years of his life he was practically blind, yet he continued to visit his many friends—and they came from all walks of life—and to keep in touch with his old students.

He was able to go to North Haven, Maine, for this, his last, summer, and although his activities were much restricted he could still sail in his beloved Penobscot waters, as he had for nearly fifty years. It is said that his boatman, on being told that Dr. Jackson was ill and could not sail with him that day and probably never would be able to do so again, retorted, "I know better; the trouble with Dr. Jackson is that he ate too many chocolates yesterday." He did indeed partly recover his health, but was forced shortly to leave North Haven and return to Chestnut Hill, where he died peacefully after another short illness. As Oliver Wendell Holmes said of James Jackson, so it may be said of his nephew, Henry, "He was a child to learn, a father to teach, a brother to help."

Honour the physician for the need thou hast of him; for the most High hath created him.

MEDICAL EPONYM

S CURVE OF ELLIS

At a meeting of the Boston Society for Medical Improvement, October 13, 1873, Professor Calvin Ellis (1826-1883), of the Harvard Medical School, discussed "The Line of Dulness in Pleuritic Effusion." His remarks were reported in the *Boston Medical and Surgical Journal* (90:13, 1874).

But, in a certain number of cases where the effusion is quite large, if an accurate line be drawn, the flatness will be found to describe a curve, gradually approaching the spine toward the base of the chest, having a space from one to three or more inches broad between the spine and the line of flatness. In this space, resonance will still be detected, and respiration heard. As the effusion increases, this line approaches nearer and nearer the spine, until the whole back becomes flat.

The attention of Ellis was called to the fact that Damoiseau had described a similar curve in "Recherches cliniques sur plusieurs points du diagnostic des épanchements pleurétiques" which was published in *Archives générales de médecine* (Series 4, 3:129-156, 1843). He said that until his attention had been called to this, he had not been aware that the point had been observed but that Damoiseau's description of this curve agreed with his observation.

An article by Ellis, entitled "The Curved Line of Pleuritic Effusion," appeared in the *Boston Medical and Surgical Journal* (95:689-697, 1876). It consists of a series of case histories and several diagrams showing a curve on the posterior aspect of the thorax in the form of an S whose tail begins at the vertebral column and whose tip descends into the axilla toward the sternum. The text contains no description of the term, the "S curve of Ellis," which was applied by Garland on pages 6 and 16 of *Pneumono-dynamics* (New York: Hurd and Houghton, 1878).

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

RAYMOND S. TITUS, M.D., *Secretary*
330 Dartmouth Street
Boston

DIABETES RESULTING IN INTRAUTERINE DEATH OF THE FETUS

Mrs. M. H., a thirty-five-year-old para III, was first seen in the office on July 5, 1929. At that time she was four and a half months pregnant.

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

The family history was non-contributory. The patient's diabetes was discovered during her second pregnancy in 1924, and three days after its discovery the patient went into diabetic coma. This pregnancy was terminated at seven months, with a stillborn child. The first pregnancy in 1922 was full term, but the baby died. Catamenia began at thirteen, were regular with a twenty-eight-day cycle and lasted three days with no discomfort. The last regular period was February 15, making the expected date of confinement November 22, 1929.

Physical examination at the time of her first visit showed a well-developed and well-nourished woman. The weight was 120 pounds. The heart was not enlarged; there were no murmurs. The lungs were clear and resonant; there were no rales. The blood pressure was 120 systolic, 66 diastolic. Vaginal examination revealed a relaxed perineum and the fundus at a level consistent with her dates. The urine contained 1.5 per cent sugar. Under the direction of a specialist in diabetes, the patient was taking 18 units of insulin daily; this dosage was later increased to 34 units.

The patient was seen frequently by both the obstetrician and the consultant, and routine samples of blood for determining the sugar concentration were taken at each visit; the lowest level was 109 mg. per 100 cc., on August 23, and the highest, 200 mg., on October 25.

On November 7 the patient seemed in good condition. The weight was 132 pounds. The blood sugar was 140 mg. per 100 cc., and the urine contained 1.1 per cent sugar. The blood pressure was 120 systolic, 70 diastolic. Abdominal examination revealed the vertex presenting, and the fetal heart was heard. On vaginal examination the cervix was soft, not open but somewhat taken up. The uterus seemed to have shrunk, although the baby had grown.

The patient entered the hospital on November 14 for better control of the diabetes. On November 15 the fetal heart was not audible. On November 19 the patient weighed 122 pounds, a loss of 10 pounds since November 7. She remained in the hospital until December 5, when labor started spontaneously. A large macerated fetus was delivered normally, although there was considerable difficulty with the shoulders. The placenta was very small, in contrast to the very large placentas which are seen in many diabetic patients.

The patient was seen in the office on January 13, 1930, for a final examination. At that time the urine had been sugar-free for five days, and she

felt very well. The weight was 116 pounds. Pelvic examination was negative.

There have been no further pregnancies.

Comment. Intrauterine death in the last few weeks of pregnancy is one of the hazards of a pregnancy complicated by diabetes, even when treated with insulin. The loss of weight of 10 pounds between November 7 and November 19 shows that the patient must have been quite edematous. The actual weight of the fetus is not in the hospital record, but inasmuch as there was considerable difficulty with the shoulders, it is fair to infer that it was a large one. The previous obstetric history surely warranted earlier delivery when it was known that the baby was alive, and the size of the baby thoroughly justified the assumption that ten days before its death the baby would have weighed enough to ensure its viability.

Experience has shown that at approximately thirty-six weeks diabetic patients should be sent to the hospital in order to be under daily supervision, unless complications demand an earlier entry.

This case illustrates the intelligent conservative treatment of a known intrauterine fatality. When the uterus harbors a dead fetus, it is wiser to leave it alone than to attempt the induction of labor.

POSTGRADUATE EXTENSION COURSES

The following sessions, given by the Massachusetts Medical Society in co-operation with the Massachusetts Department of Public Health, the United States Public Health Service and the Federal Children's Bureau, have been arranged for the week beginning October 28:

BARNSTABLE

Sunday, November 3, at 4:00 p.m., at the Cape Cod Hospital, Hyannis. Dermatitis and Eczema. Instructor: John G. Downing. Donald E. Higgins, *Chairman*.

BRISTOL NORTH

Thursday, October 31, at 4:00 p.m., at the Morton Hospital, Taunton. Obstetric Complications: With case histories and clinical problems. Instructor: Christopher J. Duncan. Lester E. Butler, *Chairman*.

BRISTOL SOUTH (New Bedford Section)

Friday, November 1, at 4:00 p.m., at St. Luke's Hospital, New Bedford. Diagnosis and Treatment of Minor Lesions of Rectum and Anus. Instructor: Neil W. Swinton. Robert H. Goodwin, *Chairman*.

ESSEX NORTH

Friday, November 1, at 4:30 p.m., at the Clover Hill Hospital, Lawrence. Dermatitis and Eczema. Instructor: J. Harper Blaisdell. John Parr, *Chairman*.

JOHNSON, DANIEL P., 8 Quincy Street, Watertown.
University of Lausanne, 1937.

KEMPT, GROVER A., United States Marine Hospital,
Brighton.
Indiana University School of Medicine, 1910.

LIPORE, JOHN J., 69 Essex Street, Marlboro.
Georgetown University School of Medicine, 1937.

LOWENTHAL, KARL, 45 Englewood Avenue, Brighton.
University of Freiburg, 1915.

MASTRANGELO, LOUIS, 572 Mt. Auburn Street, Watertown.
Middlesex University School of Medicine, 1930.

McKITTRICK, JOHN B., 60 Greenwood Avenue, West
Newton.
Harvard Medical School, 1937.

MUELLER, HANS P., 9A Ware Street, Cambridge.
Medical School of University of Koenigsberg, 1931.

NAUEN, ALICE B., 142 Sutherland Road, Brighton.
University of Hamburg, 1926.

POLLEN, DAVID A., 17 Radcliffe Road, Allston.
Middlesex University School of Medicine, 1932.

ROSS, RALPH A., 42 Englewood Avenue, Brighton.
Harvard Medical School, 1935.

SEGEL, ARNOLD L., 1959 Commonwealth Avenue, Brighton.
Harvard Medical School, 1936.

STENZEL, FRANZ R., 1580 Beacon Street, Waban.
Harvard Medical School, 1938.

SPRAGUE, JOHN S., 75 Nottinghill Road, Brighton.
Johns Hopkins University School of Medicine, 1936.

YOUNG, DAVID A., McLean Hospital, Waverley.
Harvard Medical School, 1931.

Alexander A. Levi, *Secretary*.

NORFOLK DISTRICT

ADAMS, EDWARD E., 4121 Washington Street, Roslindale.
Boston University School of Medicine, 1937.

ALLEN, EDWARD C., 26 Aspinwall Avenue, Brookline.
Tufts College Medical School, 1939.

CRAGG, GRACE T. M., Medfield State Hospital, Harding.
Dalhousie University Faculty of Medicine, 1922.

DE AGUIAR, ALCINDA P., Wrentham State School, Wren-
tham.
Oporto University, Portugal, 1925.

ELSBERG, ALBERT, 57 Thorndike Street, Brookline.
University of Berlin, 1913.

FAILLACE, FEDELE M., 44 Penniman Road, Brookline.
Royal University of Rome, 1934.

FERGUSON, ALBERT B., 1080 Beacon Street, Brookline.
Cornell University Medical College, 1917.

FRIEND, DALE G., 2 Autumn Street, Boston (Roxbury).
Harvard Medical School, 1935.

GROSSMAN, SAMUEL, 32 Wenonah Street, Roxbury.
Kansas City University of Physicians and Surgeons,
1932.

HEAVEY, THOMAS J., 4 Broad Street, Medway.
Middlesex University School of Medicine, 1922.

HOCHMAN, GEORGE V., 20 Harding Street, Sharon.
Middlesex University School of Medicine, 1934.

HOERR, STANLEY O., 159 Kent Street, Brookline.
Harvard Medical School, 1936.

HOOVER, HAROLD R., 721 Huntington Avenue, Roxbury.
University of Southern California School of Medicine,
1937.

KARPATI, OSCAR, 1477 Beacon Street, Brookline.
Royal Hungarian State "Elizabeth" University, Pecs,
Hungary, 1926.

LARSON, CARROLL B., 60 Egmont Street, Brookline.
State University of Iowa College of Medicine, 1933.

LENDGREN, CARL V., 69 Central Street, Foxboro.
Boston University School of Medicine, 1930.

LOWIS, SAMUEL, 114 University Road, Brookline.
Harvard Medical School, 1934.

MILLER, WALLACE C., Peter Bent Brigham Hospital, Rox-
bury.
Loyola University School of Medicine, 1936.

PERONA, ATTILIO C., 12 Linden Street, Norwood.
Middlesex University School of Medicine, 1934.

PIKE, GEORGE M., 368 Longwood Avenue, Roxbury.
Harvard Medical School, 1936.

PORAS, HARRY H., 208 Rawson Road, Brookline.
University of Vienna, 1929.

PROVENZANO, ROSARIO W., 62 Adams Street, Dorchester.
Tufts College Medical School, 1940.

ROTHBLATT, BERNARD W., 26 May Street, Jamaica Plain.
Tufts College Medical School, 1937.

SCHIRMER, ADELBERT F., 172 Kittredge Street, Roslindale.
Tufts College Medical School, 1939.

SCHULZ, MILFORD D., 6 Autumn Street, Boston (Roxbury).
Northwestern University Medical School, 1936.

SEALE, EARL S., 116 Riverway, Boston (Roxbury).
Tulane University of Louisiana School of Medicine,
1935.

SHWACHMAN, HARRY, 62 Elm Hill Avenue, Roxbury.
Johns Hopkins University School of Medicine, 1936.

STEAD, EUGENE A., JR., Peter Bent Brigham Hospital, Bos-
ton (Roxbury).

Emory University School of Medicine, 1932.

STONE, NATHANIEL M., 94 Naples Road, Brookline.
Tufts College Medical School, 1937.

WEATHERLY, HOWARD E., 20 Netherlands Road, Brookline.
State University of Iowa College of Medicine, 1934.

WELCH, RICHARD F., 108 Brook Road, Milton.
Middlesex University School of Medicine, 1935.

YEOMANS, ANDREW, 38 Webster Place, Brookline.
Harvard Medical School, 1935.

YOUNG, ALEXANDER, 1110 River Street, Hyde Park.
Middlesex University School of Medicine, 1934.

Frank S. Cruickshank, *Secretary*.

NORFOLK SOUTH DISTRICT

FRANKMAN, WILLIAM, 736 Hancock Street, Wollaston.
St. Louis College of Physicians and Surgeons, 1921.

MILLEN, MORRIS H., 391 Bridge Street, North Weymouth.
Middlesex University School of Medicine, 1933.

PEARLSTEIN, MAX, 447 Washington Street, Braintree.
Tufts College Medical School, 1929.

SAWYER, JOSEPH H., 1 Monatiquot Avenue, Braintree.
Massachusetts College of Osteopathy, 1927.
Middlesex University School of Medicine, 1931.

SLOANE, WILLIAM C., 15 South Main Street, Randolph.
Middlesex University School of Medicine, 1934.

WILLIAMS, ROBERT H., 56 Sycamore Road, Squantum.
Johns Hopkins University School of Medicine, 1934.

Henry H. A. Blyth, *Secretary*.

PLYMOUTH DISTRICT

- GOETZE, SIEGBERT, 815 Washington Street, Stoughton
University of Freiburg, 1909.
- McGEE, CHARLES J, 118 Hillcrest Avenue, Brockton
Harvard Medical School, 1937.
- VOGEL, FRIEDRICH, Camp Pembroke, Pembroke
University of Vienna, 1924
- WASSERUG, JOSEPH D, Lakeville.
Tufts College Medical School, 1938

Ralph C McLeod, *Secretary*

SUFFOLK DISTRICT

- ASSAD, FREDERICK C, One Bond Street, Boston
Middlesex University School of Medicine, 1934
- CHISHOLM, JULIAN F, JR, 17 Pinckney Street, Boston
Johns Hopkins University School of Medicine, 1930
- COHEN, MORRIS A, 452 Beacon Street, Boston
College of Physicians and Surgeons, Boston, 1919
- DEMING, JULIA, 406 Marlboro Street, Boston
Woman's Medical College of Pennsylvania, 1922
- DENHOFF, ERIC, Boston City Hospital, Boston
University of Vermont College of Medicine, 1938
- DIAMOND, MORRIS, c/o Lieberman, 10 Mulberry Road,
Larchmont, New York.
University of Vienna, 1920
- FARRINGTON, ROBERT F, Boston City Hospital, Boston
Harvard Medical School, 1940
- FELL, ERNEST M, 202 West Newton Street, Boston
Tufts College Medical School, 1939
- HIRSCH, OSKAR, 400 Commonwealth Avenue, Boston
University of Vienna, 1902.
- HUNTINGTON, BENJAMIN L, 311 Marlboro Street, Boston
Harvard Medical School, 1938
- IGERSHEIMER, JOSEF, c/o Mrs Grunebaum, 462 Beacon
Street, Boston
Universities of Berlin, Strassburg and Tübingen, 1904
- KASPARIAN, KARL DER, Boston City Hospital, Boston
Tufts College Medical School, 1935
- LICHTER, GERALD I, Boston City Hospital, Boston
Vanderbilt University School of Medicine, 1936
- McDONALD, EUGENE J, Boston City Hospital, Boston
Tufts College Medical School, 1937
- MILLER, CARROLL C, 131 Park Drive, Boston
Harvard Medical School, 1935
- MOLLIVER, HENRY, 258 Washington Avenue, Chelsea
Middlesex University School of Medicine, 1934
- MORTARA, FRANCO, 65 Hancock Street, Boston
University of Bologna, 1932
- PAVENSTEDT, ELEANOR, 273 Beacon Street, Boston
University of Geneva, 1929
- ROBERTS, CHARLES P, 20 Union Park, Boston
Emory University School of Medicine, 1935
- RUDIN, HAROLD W, 42 Nichols Street, Chelsea
Tufts College Medical School, 1937
- SWEETSER, PETER W, Boston City Hospital, Boston
Georgetown University School of Medicine, 1937

- WAGNER, RICHARD, 370 Commonwealth Avenue, Boston
University of Vienna, 1912
- WHITELAW, GEORGE P, 2 Primus Avenue, Boston
Harvard Medical School, 1935
- Milton Henry Clifford, *Secretary*

WORCESTER DISTRICT

- BACHRACH, SAMUEL, 6 Moore Avenue, Worcester.
Tufts College Medical School, 1938
- BLACKMAN, NATHAN, Worcester State Hospital, Worcester
University of Paris, 1936
- DEE, JOHN E, Worcester City Hospital, Worcester.
Harvard Medical School, 1938
- GOLICKMAN, LOUIS, 99 Church Street, Whitinsville
Middlesex University School of Medicine, 1933
- HARRINGTON, PHILIP V, Worcester City Hospital, Worcester.
Harvard Medical School, 1938
- HIGGINS, RAYMOND F, 39 William Street, Worcester.
McGill University Faculty of Medicine, 1937.
- HORNE, ELWOOD O, 24 Holman Street, Shrewsbury.
Tufts College Medical School, 1936
- KANT, OTTO, 10 Bruce Avenue, Shrewsbury
University of Göttingen, 1924
- LANAKENNER, PETER A, 522 Grafton Street, Worcester
Middlesex University School of Medicine, 1933
- MacDONALD, WILFRED D, Belmont Hospital, Worcester
Tufts College Medical School, 1938
- MEYERSON, FRANZ, 753 Pleasant Street, Worcester.
University of Berlin, 1915
- POTTS, WILLIAM L, Worcester County Sanatorium, Worces-
ter.
Western Reserve University School of Medicine, 1933
- ROSENBLUM, HARRY A, Brimfield Road, Fiskdale
Kansas City University of Physicians and Surgeons,
1932.
- SALOMON, ROBERT, 138 Elm Street, Worcester.
University of Frankfurt, 1926
- SMITH, EUGENE F, 6 Park Terrace, Milford
Tufts College Medical School, 1935
- STEVENS, HERMAN D, Worcester County Sanatorium,
Worcester.
Jefferson Medical College of Philadelphia, 1938
- TELL, ABRAHAM B, 135 Chandler Street, Worcester.
Kansas City University of Physicians and Surgeons,
1931.

George C Tully, *Secretary*

WORCESTER NORTH DISTRICT

- GROSSMAN, MYER J, 599 Main Street, Athol
Middlesex University School of Medicine, 1933
- VERSTANDIG, CHARLES C, Fort Devens
University of Tennessee College of Medicine, 1939
- Edward A Adams, *Secretary*.

NEW HAMPSHIRE MEDICAL SOCIETY

DEATH

SHELDON—HAROLD E. SHELDON, M.D., of Troy, died at his home on September 24, at the age of forty.

Dr. Sheldon was born on October 24, 1899, in West Brattleboro, Vermont, a son of John E. and Cora (Brown) Sheldon. He received his degree from Boston University School of Medicine in 1936. Dr. Sheldon was a fellow of the American Medical Association.

He is survived by his widow and two brothers, Elmer H., of Lyme, and Harley F., of Hinsdale.

VERMONT STATE MEDICAL SOCIETY

VERMONT NEWS

BURLINGTON FREE DISPENSARY

The Burlington Free Dispensary will offer more coordinated and more convenient service to its patients, drawn from the underprivileged of Burlington, when it opens for 1940-41 under the management of its new full-time medical director, Dr. Theodore H. Harwood, who is also assistant professor of medicine in the University of Vermont College of Medicine. Dr. Harwood will be the first to manage the dispensary under a full-time arrangement. Under his direction, each new patient will pass through the Admissions Clinic for diagnosis before being referred to other clinics for treatment.

The times set for clinics are earlier, in order that patients may be given more prompt attention. Dr. Harwood, in addition to overseeing the whole program of clinics, will have direct supervision of the Medical Clinic, which will be held every afternoon at 2 p.m.

The Burlington Free Dispensary is operated by the City of Burlington through the Charities Department and by the University of Vermont College of Medicine. Its schedule of clinics includes surgery, medicine, pediatrics, gynecology, obstetrics, mental hygiene (for children up to eighteen), orthopedics surgery, urology, dermatology, allergy, physiotherapy, eye, ear, nose and throat, and syphilology. There is a State-operated clinic for chest diseases, and the new Squint Clinic, for the correction of cross eyes.

MISCELLANY

HARVARD UNIVERSITY MONOGRAPHS IN MEDICINE AND PUBLIC HEALTH

With the purpose of encouraging the publication of books and monographs of scientific importance by members of the Harvard Medical School and the Harvard School of Public Health, and of adding to the distinction both of the two schools and of the Harvard University Press by publishing under their auspices a noteworthy series of monographs in medicine and public health, a sum of money has been provided, to be used for an experimental period of three years, as a revolving publication fund. An editorial committee has been appointed to administer this fund, and to select books and monographs to be included in a series entitled *Harvard University Monographs in Medicine and Public Health*.

The members of the committee are Dr. A. Baird Hastings, chairman, Dr. Walter B. Cannon, Dr. J. H. Means, Dr. S. Burt Wolbach and Dr. Katherine R. Drinker, executive secretary.

Members of the faculties of the medical school and of the school of public health who have written, or who contemplate writing, books or monographs suitable for such a series have been invited to consult with the Editorial

Committee and to submit their manuscripts for inclusion in the series. If financial assistance for publication of a book is required, the committee is authorized, after arrangement with the Harvard University Press, to use the publication fund for this purpose.

In order to further the economical manufacture and the successful sale of books in the monograph series, the Editorial Committee is prepared to supply to authors—via its executive secretary—consulting advice on the proper preparation of manuscripts for publication, and to make sure that announcements of books published under its auspices are widely circulated to especially interested groups.

Number 1 of the series—to be published in November—will be *The Endocrine Function of Iodine* by Dr. William T. Salter.

A. M. A. RADIO PROGRAM

"Doctors at Work" is the title of the sixth annual series of dramatized radio programs to be presented by the American Medical Association and the National Broadcasting Company.

The series will open Wednesday, November 13, and will run for thirty consecutive weeks, closing with a broadcast from the meeting of the American Medical Association at Cleveland, on June 3, 1941. The program is scheduled for 10:30 p.m. Eastern standard time (9:30 Central; 8:30 Mountain; 7:30 Pacific) over the Blue Network and other stations of the National Broadcasting Company and Canadian stations.

The programs will dramatize what modern medicine offers the individual in the way of opportunities for better health and the more successful treatment of disease. Incidental to this main theme, the programs will explain the characteristics of the different fields of modern medicine and its specialties.

Descriptive posters for local distribution may be had gratis from the Bureau of Health Education, American Medical Association, 535 North Dearborn Street, Chicago. Program titles will be announced weekly in the *Journal of the American Medical Association* and monthly in the *New England Journal of Medicine*.

NOTES

The Massachusetts Society for Mental Hygiene announces a new bulletin, *The Mental Health Sentinel*, the first number of which is being published late in October. This new magazine, which supersedes the society's monthly bulletin, is a quarterly of 24 pages and is aimed to interest all groups in the community; it will contain special articles of interest to physicians. The subscription price is \$1.00 per year (four issues).

The University of California has recently announced that Dr. Walter B. Cannon, George Higginson Professor of Physiology at the Harvard Medical School, will be Charles M. and Martha Hitchcock Professor during February, 1941.

Three National Scholarships, the outstanding awards to students entering the Harvard Medical School this fall, were recently announced by Harvard University. The recipients are James S. Clarke, of La Grange, Illinois, S.B. Harvard '40; Martin E. Flipse, of Douglaston, Long Island, New York, A.B. Hope College '40; and Winsor C. Schmidt, of Rye, New York, who attended Yale. This is the fourth year of the medical school's National Scholarship plan, which is similar to that introduced in Harvard College in 1934, and subsequently adopted by

the Graduate School of Arts and Sciences and the Graduate School of Design. Winners of the scholarships who maintain honor records continue to hold the awards until graduation

NOTICES

BOSTON DOCTORS SYMPHONY ORCHESTRA



The Boston Doctors' Symphony Orchestra will rehearse under Alexander Thiede, former concert master with the Cleveland Symphony Orchestra, every Thursday at 8 30 p m Those interested in becoming members should com

municate with Dr Julius Loman, Pelham Hall Hotel, Brookline (BEA 2430)

PETER BENT BRIGHAM HOSPITAL

A joint medical and surgical clinic at the Peter Bent Brigham Hospital will be held on Wednesday, October 30, from 2 to 4 p m Drs E C Cutler and Soma Weiss will speak, their subject being "The Unconscious Patient" A clinicopathological conference, conducted by Dr Elliott C Cutler, will take place from 4 to 5 p m

Physicians and students are cordially invited to attend

MASSACHUSETTS GENERAL HOSPITAL

A meeting of the Hospital Research Council will be held in the Ether Dome of the Massachusetts General Hospital on Tuesday, October 29, at 5 00 p m

PROGRAM

Studies Pertaining to the Physiologic and Therapeutic Effects of Low Temperature

Clinical Aspects and Renal Function Dr John H Talbot

Constituents of Blood and Respiratory Functions Drs D Bruce Dill and William H Forbes

Therapeutic Considerations in Schizophrenia Dr Kenneth J Tiltson

JOSEPH H PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston
Lecture Hall, 9-10 a m

MEDICAL CONFERENCE PROGRAM, NOVEMBER-DECEMBER

Friday November 1—Lupus Erythematosus Case report and pathological discussion Dr H E MacMahon.

Saturday, November 2—Hospital Case Presentation Dr S J Thannhauser

Tuesday, November 5—Management of Pulmonary Abscess Dr R H Betts

Wednesday, November 6—Hospital Case Presentation Dr S J Thannhauser

Thursday, November 7—Carcinoma of the Pancreas Clinical review of cases. Dr E P Engleman

Friday, November 8—Experimental Studies in Pernicious Anemia Dr M M Wintrobe

Saturday, November 9—Hospital Case Presentation Dr S J Thannhauser

Tuesday, November 12—Narcolepsy A review and presentation of cases Dr W F Murphy

Wednesday, November 13—Hospital Case Presentation Dr S J Thannhauser

Thursday, November 14—Motion Picture Ovulation and Effects of Pregnant Mares Serum—Gonadogen

Friday, November 15—Meniere's Disease. Dr Donald Munro

Saturday, November 16—Hospital Case Presentation Dr S J Thannhauser

Tuesday, November 19—The Present Status of Urinary Tract Calculi Dr H W Sulkowitch.

Wednesday, November 20—Hospital Case Presentation Dr S J Thannhauser

Thursday, November 21—Dysmenorrhea Dr L E Phineuf

Friday, November 22—The Formation of Biliary Calculi Dr L Lichtwitz

Saturday, November 23—Hospital Case Presentation Dr S J Thannhauser

Tuesday, November 26—X ray Demonstration Dr A Ettinger

Wednesday, November 27—Hospital Case Presentation Dr S J Thannhauser

Friday, November 29—Marble Bone Disease Dr Albert Frank

Saturday, November 30—Hospital Case Presentation Dr S J Thannhauser

SUFFOLK DISTRICT MEDICAL SOCIETY

There will be a meeting of the Suffolk District Medical Society in the Princess Ballroom of the Hotel Somerset, 400 Commonwealth Avenue, on Wednesday, October 30

PROGRAM

12 00 m Luncheon, gratis to those members notifying the secretary at least twenty four hours in advance.

12 30 p m Stated Meeting

1 00 p m Lessons for Physicians and Surgeons from the Army and Navy Capt J J A McMullen, MC, U S N, Col J J Reddy, MC, U S A, and Lt Col A R Bolling, GSC, U S A

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	ORTHOPEDIC CONSULTANT
Lowell	November 1	Albert H Brewster
Salem	November 4	Harold C. Bean
Haverhill	November 6	William T Green
Gardner	November 12	Mark H Rogers
Brockton	November 14	George W Van Gorder
Worcester	November 15	John W O Meara
Pittsfield	November 18	Francis A Slowick
Northampton	November 20	Garry deN Hough, Jr
Hyannis	November 26	Paul L Norton
Fall River	November 27	Eugene A McCarthy

NEW ENGLAND HEART ASSOCIATION

There will be a special meeting of the New England Heart Association at the Boston Medical Library in honor of the late Dr Maude E Abbott on Friday, November 8, at 8 15 p m

PROGRAM

In Honor of Dr Maude E Abbott
Dr Abbott and McGill University Dr Charles S Martin, of Montreal
Her Contribution to Cardiology Dr Paul D White.

Personal Reminiscences. Dr. Emanuel Libman, of New York City.

Changes Which Occur During Life in Patients with Congenital Malformations of the Heart. Dr. Helen B. Taussig, of Baltimore.

Interested physicians and medical students are invited to attend.

NEW ENGLAND PEDIATRIC SOCIETY

There will be a meeting of the New England Pediatric Society on Wednesday, October 30. The clinical presentation will be held at the Cheever Amphitheater, Dowling Building, Boston City Hospital, and all the other events at Longwood Towers, Brookline.

PROGRAM

4:00 Dry Clinic: Dr. Edwin H. Place and his associates.

6:00 Refreshments.

7:00 Dinner.

8:00 "When Bobby Goes to School," a moving picture. The Prevention, Diagnosis and Treatment of Some of the Common Contagious Diseases. Dr. Philip M. Simson, visiting physician, Willard Parker Hospital, New York City.

THOMAS WILLIAM SALMON MEMORIAL LECTURES

The Salmon Committee on Psychiatry and Mental Hygiene invites the members of the medical profession and their friends to the Eighth Series of Thomas William Salmon Memorial Lectures.

This series will be given by Dr. Nolan D. C. Lewis, director of the New York State Psychiatric Institute, and professor of psychiatry at Columbia University. The lectures will be given on successive Friday evenings, November 8, 15 and 22, at 8:30 p.m., at the New York Academy of Medicine, 2 East 103rd Street, New York City. Dr. Lewis will speak on "The Pathway of Research in Psychiatry."

UNITED STATES CIVIL SERVICE COMMISSION

The Civil Service Commission announces that enough applications have been received to meet the prospective need for temporary and part-time civilian medical officers in connection with the Army expansion.

The commission calls attention to the fact, however, that there is an urgent need for medical officers and senior and associate medical officers to fill permanent positions in other agencies. Applications will be received until further notice. The positions pay from \$3200 to \$4600 a year. Fourteen specialized branches of medicine are included.

There is also an urgent need to fill junior medical officer positions at \$2000 a year at St. Elizabeths Hospital, Washington, D. C.

Full information and application forms for these examinations may be obtained at the office of the Secretary, Board of United States Civil Service Examiners at any first- or second-class post office, from the United States Civil Service Commission, Washington, D. C., or from any of the commission's district offices.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING SUNDAY, OCTOBER 27

MONDAY, OCTOBER 28

12 15-1 15 p m Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

TUESDAY, OCTOBER 29

*9-10 a m Food Allergy. Dr. E. A. Brown Joseph H. Pratt Diagnostic Hospital

12 15-1 15 p m Clinicorontgenological conference Peter Bent Brigham Hospital amphitheater.

5 p m Hospital Research Council. Massachusetts General Hospital

WEDNESDAY, OCTOBER 30

*9-10 a m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital

*12 m Clinicopathological conference Children's Hospital.

*2-4 p m The Unconscious Patient Drs. E. C. Cutler and S. Weiss Peter Bent Brigham Hospital

4-5 p m. New England Pediatric Society Boston City Hospital, Cheever amphitheater

6-8 p m. New England Pediatric Society. Longwood Towers, Brookline.

THURSDAY, OCTOBER 31

*8 30 a m Combined clinic of the medical, surgical orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital, at the Peter Bent Brigham Hospital

*9-10 a m Fever Therapy in Diseases of the Nervous System Dr. S. H. Epstein. Joseph H. Pratt Diagnostic Hospital

FRIDAY, NOVEMBER 1

*9-10 a m Lupus Erythematosus Case report and pathological discussion. Dr. H. E. MacMahon Joseph H. Pratt Diagnostic Hospital

SATURDAY, NOVEMBER 2

*9-10 a m Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*Open to the medical profession.

NOVEMBER 1-30 — Joseph H. Pratt Diagnostic Hospital. Page 691.

NOVEMBER 8 — New England Heart Association. Page 691

NOVEMBER 8, 9 — Society for Research in Child Development Page 648, issue of October 17.

NOVEMBER 8, 15 and 22 — Thomas William Salmon Memorial Lectures Notice above

NOVEMBER 13, 14 — New England Postgraduate Assembly. Cambridge, Massachusetts

NOVEMBER 14 — Pentucket Association of Physicians Page 263, issue of August 15.

NOVEMBER 14 — American Conference on Industrial Health Page 648, issue of October 17

NOVEMBER 15 — Massachusetts Society for Mental Hygiene. Page 648, issue of October 17

DECEMBER 27-29 — National Convention of the Association of Medical Students, Boston.

JANUARY 4, 1941 — American Board of Obstetrics and Gynecology. Page 1064, issue of June 20.

MARCH 8 — American Board of Ophthalmology. Page 201, issue of August 1.

APRIL 21-25 — American College of Physicians Page 1065, issue of June 20

MAY 21, 22 — Massachusetts Medical Society, Boston.

JUNE 2-6 — American Medical Association. Cleveland, Ohio.

DISTRICT MEDICAL SOCIETIES

FRANKLIN

NOVEMBER 12.

JANUARY 14.

MARCH 11.

MAY 13.

Meetings will be held at 11 a.m. at the Franklin County Hospital, Greenfield.

NORFOLK

OCTOBER 29 — Page 648, issue of October 24.

SUFFOLK

OCTOBER 30 — Page 691.

NOVEMBER 7 — Censors' meeting. Page 305, issue of August 22.

JANUARY 29 — Page 604 issue of October 10
 APRIL 30 — Page 604 issue of October 10

WORCESTER

NOVEMBER 13 — Grafton State Hospital Grafton
 DECEMBER 11 — St. Vincent Hospital Worcester
 JANUARY 8 1941 — Worcester City Hospital Worcester
 FEBRUARY 12 — Worcester State Hospital Worcester
 MARCH 12 — Memorial Hospital Worcester
 APRIL 9 — H. I. Newman Hospital Worcester

Supper at 6:30 p.m. followed by a business meeting and scientific program

BOOK REVIEWS

On Oxidation, Fermentation, Vitamins, Health and Disease By Albert V. Szent-Gyorgyi, M.D., Ph.D., D.H.C. 12", cloth, 109 pp. Baltimore: Williams & Wilkins Company, 1939. \$2.00

This formidable title embraces five Abraham Flexner Lectures given in 1939 at Vanderbilt University School of Medicine and published for the University. The distinguished 1937 Nobel prize winner and professor of medical chemistry at the University of Szeged, Hungary, has summarized in simple but vivid and personal language the results of his investigations on biological oxidation, pursued during the past fifteen years. It was a difficult task to present such a highly technical subject to a general medical school audience, but Dr. Szent-Gyorgyi has done it in a fruitful and inspiring way, and with the brevity of about a hundred printed pages.

The first lecture deals with the problem of biological oxidation — the long series of controlled chemical reactions whereby carbohydrates are oxidized, through the agency of the animal's specific enzymes, so gradually that at every stage the animal cell can utilize the small quantity of energy liberated.

Muscle respiration is the subject of the second lecture. Here another similar chain of oxidations is traced, each reaction being made possible by a specific enzyme or catalyst of the animal cell.

The third lecture concerns fermentation and its relation to oxidation. Fermentation is essentially an anaerobic molecular rearrangement with the liberation of quantities of energy much smaller than those concerned in oxidation, but still sufficient to support life in the form of bacteria and yeasts, and of use in muscular activity in man. One of the reactions involved in muscle fermentation is decarboxylation. Curiously, the coenzyme decarboxylase, concerned in this reaction, is found to be identical with phosphorylated vitamin B₁. Thus vitamin B₁ deficiency becomes explicable in terms of interference with the normal decarboxylation in muscle.

In the fourth lecture, on vegetation oxidations, the author mentions his discovery of a substance concerned with plant oxidation systems, which later proved to be ascorbic acid. Szent-Gyorgyi thus became the father of vitamin C.

The concluding lecture, on vitamins, health and disease, begins by asking why man cannot synthesize in his body the substances we call vitamins. Some of them can be made by other animals, notably vitamin C by the rabbit, and it is suggested that our long tropical ancestry, with its continuous supply of green plants, has lost us the ability to make this substance.

In expounding his general theory of health and disease, Szent-Gyorgyi unfortunately goes off the deep end. He paints a picture of man in his natural jungle environment, perfectly adapted to it and therefore perfectly healthy.

As a more modern counterpart he cites the island of Tristan da Cunha, where man of our own race lives a natural life and knows no disease. Again, he states: "Tuberculous patients are sent to the mountains and it is known that no tuberculosis exists above 9000 feet. [The mountain air] is simply the air we are made for, and if we have what we are made for there will be no tuberculosis." In other words, practically all disease is merely maladjustment to the present environment.

On the whole this is a very stimulating and valuable little volume, heartily to be recommended.

Let's Talk About Your Baby By H. Kent Tenney, Jr., M.D., with a foreword by Joseph Brennemann, M.D. Second edition. 12", cloth, 115 pp. with 13 illustrations. Minneapolis: University of Minnesota Press, 1940. \$1.00

Books dealing with the problems of the baby's first year are relatively numerous and for the most part sound but from the standpoint of reading, most of them have little appeal. This one, however, aims to be enjoyable as well as instructive, and this end has been surprisingly well achieved. Information regarding food, furniture, clothing, habits, parents, doctors and diseases is presented with a most welcome freedom from dogmatism and rigidity. It should be helpful to a young mother in many ways, not the least of which will be to relieve the notion that in bringing up her young one she will have to learn and conform to a regime as inflexible as the edicts of Media and Persia. This book is highly recommended.

Your Marriage: A Guide to Happiness By Norman E. Himes, B.A., M.A., Ph.D. 8", cloth, 434 pp., with 12 charts. New York: Farrar and Rinehart, 1940. \$3.75

The author has succeeded in living up to the claims of the omnibus on the book jacket by making available a discussion of the psychological, the physical and the economic aspects of marriage.

Directed with greatest effectiveness at the educated and unattached young person, this book offers an objective and factual approach to happiness in marriage. It is completely documented, and never fails to differentiate fact and opinion. The reprinting of the actual tests to predict marital happiness and adjustment, with instructions for self-scoring, forms an important part of the book. The author bases much of his material on the results of these tests. Therefore the reader should be constantly aware of the author's point of view, that is, unfortunately, some of the newer scientific results run counter to not a few of the widely accepted opinions of authorities. Wherever there has been a conflict between revolutionary principles statistically determined on a small sample and the judgment and conclusions of experts based upon their wide knowledge of human nature, history, clinical experience and science in general, I have accepted the latter. Until such time as there are corroboratory studies on marriage besides those by Professor Terman and by Professors Burgess and Cottrell, I think we should view such studies with sympathy but caution" (page 10).

While it offers nothing new on sex life in marriage, sexual adjustment and the art of love, to which two chapters are devoted, the book does include an excellent bibliography on sexual enlightenment, and weighs the advantages of reading as opposed to personal counseling in specific situations. Equally valuable is the listing of counseling centers.

The approach to the advantages of early marriage is put forth satisfyingly and realistically, and the chances

of its success are probably enhanced by a consideration of the factors of background and personality. Perhaps the most unique and valuable contribution is the discussion of finances, budget, credit, insurance, housing and the general job of being a consumer. Added to this is the fact that such subjects are ably discussed along with the more usual chapters on emotional and physical adjustment. To the normal young person whose goal is marriage and whose education has fitted him or her to prepare for it at least as painstakingly as for any other situation, the book may indeed be "a guide to happiness."

Fractures and Other Bone and Joint Injuries. By R. Watson-Jones, M.Ch., B.Sc., Ch.B., M.B., M.R.C.S. (Eng.). 8°, cloth, 723 pp., with 1040 illustrations. Baltimore: Williams & Wilkins Co., 1940. \$13.50.

This book includes orthopedic practices which have been developed in many parts of the world. The author's breadth of vision and experience can best be understood by reading the first chapters on the physiology and pathology of osseous tissues. A mastery of these principles enables one to establish a set of criteria to evaluate new methods. With this background the author has searched widely and assembled much of the best thought on orthopedic problems.

The necessity for complete immobilization of fractures is continually stressed; but the author also emphasizes the dangers of overimmobilization and the attendant morbidity caused by unnecessary stiffness in joints. The exactness of his descriptions in the treatment of individual fractures and joint diseases enables one to follow his methods closely. There is a timely chapter on the omnipresent backache and the importance of prolapsed intervertebral disks in chronic sciatica. The Winnett-Orr treatment of compound fractures and the aftercare following the original cast are described in detail.

There are a great number of excellent x-ray pictures and diagrams for the illustration of the text. Another feature of the book is a comprehensive and up-to-date bibliography.

It was the English school of surgeons who gave the greatest impetus to orthopedic surgery during World War I, and this book shows how well they have continued their leadership in this field during peacetime.

The Journal of Gideon Mantell, Surgeon and Geologist, Covering the Years 1818-1852. Edited, with an introduction and notes, by E. Cecil Curwen. 8°, paper, 293 pp. London: Oxford University Press, 1939. \$4.25.

Dr. Mantell was a surgeon and general practitioner who lived in Lewes, England, and kept a diary from 1818 to 1852. In addition to his practice, he carried on extensive investigations concerning the geology of the district about Lewes, which culminated in a book, *The Fossils of the South Downs*, published in 1822. He frequently traveled to London at the time when he was intimate with Sir Charles Lyell, Thomas Hodgkin and others. There are excellent descriptions of the early meetings of the British Association for the Advancement of Science. Through the efforts of his friend, Professor Silliman, he received the degree of LL.D. from Yale University in 1834. Dr. Morton, of Philadelphia, dedicated a geological work to him. Dr. Mantell's geological collection was sold to the British Museum. In medicine, he contributed frequent papers to the *Lancet*. After leaving Lewes, he practiced for many years in Clapham, and became a member of the Royal Society. His journal reflects the medical and scien-

tific life of England one hundred years ago, as recorded by a physician, who, in addition to his practice of medicine, was a scientist of note. This is an important historical document, carefully edited.

Cancer in Childhood. By Harold W. Dargeon, M.D. 4°, cloth, 114 pp., with 42 illustrations and 6 tables. St. Louis: C. V. Mosby Company, 1940. \$3.00.

This book represents the communications of eleven authors, and it aims to cover not merely cancer proper but all the malignant tumors which may occur in the early years of life. The observations were made at the Memorial Hospital for the Treatment of Cancer and Allied Diseases in New York City, with the purpose of correcting the rather general impression that cancer in youth is a matter of no very great importance because of its rarity. The greatest number of facts and conclusions that can now be assembled are collected and published in this book; they should be of interest to all who care medically for the young. There is nothing of finality in the presentation, nor is there intended to be, only the hope of awakening interest in further study.

An Introduction to Medical Genetics. By J. A. Fraser Roberts, M.A., M.B., D.Sc., F.R.S.E. 8°, cloth, 266 pp., with 94 illustrations. London: Oxford University Press, 1940. \$4.50.

Practitioners of medicine rarely have the inclination to study a book on mammalian genetics. For such gentlemen, Dr. Roberts offers the structural framework on human genetics. The subject is addressed to the senior student and to the clinician; it deals with the human subject as observed in the community, in medical practice and in the hospital. Some of the entities considered are: brachydactyly, alkaptonuria, Osler's disease (multiple telangiectasia), night blindness, Huntington's chorea, albinism, hemophilia, blood groups and so forth. There is an excellent chapter on heredity as a factor in the causation of disease. The book closes with notes on the recording of genetic data.

It seems to the reviewer that this is a timely book, since increased emphasis is being placed on hereditary constitution as one of the factors to be considered in discussions on the causation of disease, as presented by teachers in medical schools and in hospitals.

An Anatomical Analysis of Sports. By Gertrude Hawley, M.A. 8°, cloth, 191 pp., with 97 illustrations. New York: A. S. Barnes & Company, 1940. \$3.00.

This is another Barnes book written primarily for physical educationists and coaches. The careful description of muscular action and joint function is well done, and although one cannot entirely agree with everything the author writes, on the whole it is a careful analytical study. One who is not a physical educationist could definitely take issue with the author in some of her descriptions, listings and classifications of muscle groups with definite functional action.

Admirable analytical descriptive material, well correlated, is presented for the individual sports discussed, namely, archery, baseball, basketball, horseback riding, fencing, field hockey, football, golf, swimming and diving, tennis and track, field and winter sports. This is interesting to all those who are concerned in the detail of this material.

The New England Journal of Medicine

Copyright, 1940, by the Massachusetts Medical Society

VOLUME 223

OCTOBER 31, 1940

NUMBER 18

THE CARE OF THE PATIENT*

CHARLES R. AUSTRIAN, M.D.†

BALTIMORE

IT WAS a happy idea to have an annual lecture here on "The Care of the Patient," for, as your chairman, Dr. Bauer, has phrased it, it affords an opportunity "to emphasize many of the things which the student cannot possibly be aware of because he has never practiced." Perhaps those responsible for the thought were impressed with the impossibility of arranging a curriculum so inclusive that it would comprise all that a medical man should know. Perhaps they received this impression from their personal experience, mindful of how at graduation they ceased abruptly to be good medical students and were at once poor doctors; or it may be that they came to their conclusion by their observation of practicing colleagues or by what the latter told them.

The concept cherished through the ages that a physician is worthy and able to serve the suffering is the ideal of the doctor today. All that has been done and is being done in the study of the cause, the prevention, the manifestations and the evolution of disease has had and still has for its ultimate aim the palliation and the cure of sickness.

The engineer, the mechanic, the artisan of every sort, works with materials of known composition, quality and strength, of standardized assembly and number. If faults develop, he has the means to determine their causes, to repair and to replace parts that have become worn or have deteriorated, to relocate the machine. You, as physicians, will deal with a structure more complex, less understood, with a great many parts, all of which are not only self-wearing but must be self-repairing, and the evidences for the defects of which may be quite elusive. To find the individual faults and to piece them together in a way to disclose the damage in its entirety will often tax you more than it does a detective to find the clues and to procure the incriminating evidence of a cleverly executed crime,

and to remedy them will be as difficult as it would be for a prosecutor to convict a powerful politician in a partisan-controlled community. You may be skilled in the sciences, facile with chemical, physical, biological and many other technics, you may know the physical manifestations of many diseases, you may contribute to the store of knowledge and be a medical scientist, but you will not be a physician until you have developed what has been called a clinical sense. This is an acquired faculty based subtly but soundly on a broad knowledge, a retentive memory, a discriminating and orderly habit of mind, combined with an understanding of mankind.

What is a patient? Literally, he is "one who suffers, bears or endures—a sick person." Practically, he is an individual who is under medical or surgical treatment. The diseased attract the interest of the physician; the patient commands his solicitous care that is helpful in so far as it is founded securely on a sympathetic understanding of the individual and a knowledge of medicine. In the study of disease, the basis of the patient's ills, progress has been slow and difficult. The study of structure, of function, of physical and emotional symptoms, of reactions to all external stimuli and to empirical treatment initiated a comprehension of illness. In the course of time, many sciences became the assistants of medicine, so that diagnosis and treatment were established on a surer foundation. Sometimes, it has seemed, these helpers have altered the perspective and dimmed the aims of the helped by placing too much emphasis on the objective aspects of disease, too little on the subjective. Perhaps this was inevitable as the trends of thought changed, as the worker in the laboratory replaced the clinician in the study of medical problems. It is not surprising that instruments of precision, methods of chemical or physical analysis or other types of laboratory investigation have been sup-

*A George W. Gay Lecture on Medical Ethics, presented at the Harvard Medical School, April 15, 1940.

†Associate professor of medicine, Johns Hopkins University, visiting physician, Johns Hopkins Hospital, and physician in-chief, Sinai Hospital.

planting instead of supplementing the clinical study of the patient. Although these exact procedures are helpful, they are only accessories in the care of the sick man, for clinical problems emanate from the clinic, and there the solution of them must be tested. Occupied by his interest in and respect for scientific methods, the doctor is apt to become unmindful of the fact that the beginnings of disease are insidious, cause little disturbance of function and give no detectable signs. Sooner or later they lead to the development of symptoms; the affected person feels that he is not well, and he seeks advice first at a time when the most careful examinations known will fail to disclose any objective cause for his discomfort. His subjective sensations are the earliest manifestations of ill-health. How little many of them are understood and how often they are misinterpreted! Who among physicians has not labeled such a complainer without abnormal signs a hypochondriac, a neurotic or even a malingerer, only to be embarrassed later to find that disease had developed and made him ready to subscribe to the saying of the late William S. Thayer, "After twenty years I relabel my neurotics my diagnostic errors." How many of you third-year and fourth-year students have not already on being asked when you had left an out-patient department or ward, "What did you see today?" replied with disgust, "Just another neurotic"? There are many people with what are called functional disorders. Many have no organic disease, but until precise and careful studies shall have established all the causes and the full significance of such common sensations as pain, weakness, dizziness, palpitation and a host of others, the differentiation between a neurosis and an early stage of physical disease may be impossible and may necessitate frequent critical review. It may take several years and some sad experiences to teach the full meaning of a subjective symptom.

You have been taught that the proper care of the patient should start at the first meeting with him; that from the beginning he must be regarded not merely as an example of some disease, not solely a problem for research, but as an animate being with all the attributes of man, psychic and somatic, liable to any or all the ills to which man is heir. In addition to his tissues and organs, he is endowed with a capacity to feel, to think and to act as an individual. He has an endurance, a reserve or a resistance peculiar to himself. He is identical with none other.

Put at ease, encouraged freely to tell what troubles him, listened to with sympathy, questioned intelligently, impressed by your interest in him and

in his difficulty, he will disclose shortly the type of man he is; than this there is no single datum more valuable as a guide to a correct diagnosis and to proper treatment. However, if your attitude seems detached or cold, or if your questions are badly phrased, his response may be incomplete or worded so as to conceal essential facts. Through the consideration of man as a psychobiological unit, the first manifestations of emotions or disease in different individuals have been established. Just as anxiety or fear causes weakness in one, diarrhea or diuresis in another, and tachycardia or palpitation in a third, so also anoxia of the heart muscle may cause pain in some, and dyspnea or faintness without pain in others who are less sensitive; or two duodenal ulcers apparently identical as to size and activity may be responded to very differently by two hosts. By the same token, it is scarcely necessary to predicate that there are different strains of tubercle bacilli in order to explain why localized tuberculosis of the lungs manifests itself by a general constitutional reaction or by symptoms referable to a dysfunction of the thoracic, abdominal or pelvic organs. Thus, even though the etiology of a disease be unitary, its manifestations may vary greatly, and the factors responsible for an atypical response cannot be determined except through a better understanding of the patient as a whole.

To those of you who have already served an apprenticeship in this school, these facts and those that follow are not new, but it should be emphasized that your practice while undergraduate students has been different in some measure from that of the doctor in the outside world. In the clinic, a patient may perhaps be content to be a case of this or that, to be the hub of your investigation or material for instructing you. He came to the hospital with the idea that his problem demanded compliance with conditions there, and he has faith that such compliance will be helpful to him. In the consulting room or in the home, the applicant for care regards himself as your patron; he has chosen you by chance, on the recommendation of a friend, or because of some particular aptitude he has heard that you possess. No "case," no material, no subject for demonstration, he expects what all patients in hospitals or outside them should and can receive—your personal attention, your solicitude, as well as the study that is his by right. Your professional standing in the hospital may be high despite a neglect of and a proper regard for the patient as an individual. Your success in private practice may be sacrificed solely through want of it. Beyond peradventure, the attention given to the patient's sensations, to his re-

sponses to his environment as well as to his infirmities, is often as important in determining the outcome of many minor ailments as are the remedies prescribed, and it is as vital in promoting the comfort of the gravely sick as is any form of symptomatic treatment. You yourself will want to give this attention and will delegate it to another reluctantly, and then only to someone better trained than you to give it; for to surrender the opportunity directly to mobilize the forces and to direct the battle to restore a needed adjustment will be to forego the thrill of attuning a personality.

Your study of the patient should be skillful and intelligently complete, not needlessly comprehensive. If every known examination were made of every patient, much that goes undiscovered in diagnosis might be revealed, but who could survive the ordeal physically, psychically or financially? Certainly, a sufficiently complete diagnostic survey should be made of each condition until its nature is clear, but the routine performance of needless tests indicates a lack of skillful observation and thinking, dulls clinical acumen, penalizes patients, wastes time and material, and gives the public an incorrect view of the cost of sound medical care. Do not misinterpret—let the study be thorough, expand it as far as need be to solve a given riddle or to advance knowledge, but do not expect mere elaboration of procedure to replace your clinical sense, nor rely on it to impress your colleagues or your clientèle. It is not so long since an aged colored woman who entered a large municipal hospital because of a "misery" in her back underwent studies of her metabolism, of her renal function, of the chemical constituents of her blood, and x-ray examinations of her spine and kidneys, when a simple pelvic examination made more promptly would have shown that the cause of her symptoms was a sizable carcinoma of the cervix.

Even at the risk of being considered backward, learn better to look and to see. Observation, still the most informative of all clinical methods, seems so simple that it is practiced too little. Yet what other means gives an insight so quickly into a diagnostic and therapeutic problem? To the seeing eye, a glance reveals the apparent age, sex, size, color, nutrition, mood, changes of the skin (native or factitious), comfort or discomfort, and clues of circulatory, pulmonary, abdominal and endocrine disease, even of habits past and present and of occupation. To the trained eye, all that is seen is pregnant with information. To the eye that has not learned to see, it is barren. To the former, there is opened a vista of diagnostic, thera-

peutic, even prognostic data that no other single procedure could reveal. Osler used to have the third-year students at Johns Hopkins University School of Medicine read Voltaire's "Story of Zadig," and then have them practice that oriental Hawshaw's method of finding the horse thief in seeking to detect the robber of health.

How quickly accurate observation helped to solve one man's problem! A man about thirty-five years of age, had been quite well until several weeks before he came to the dispensary because he had developed abdominal cramps, tenesmus and a watery diarrhea. Daily the severity of his symptoms had increased. He had lost weight and strength. The examinations made in order to discover the cause of the illness would have been many had not the presence of numerous silvery specks on the skin and hair aroused interest. It was a simple matter to ascertain that they came from the cheap wallpaper newly hung in his bedroom; with the knowledge that such wallpaper contains arsenic, it was easy to infer that the patient had arsenical poisoning, and he was cured by being moved to another room. Again, in the case of a young girl with mitral stenosis, direct inspection revealed multiple telangiectases on the skin and nasal mucosa, which readily explained the patient's recurring epistaxis, and thus dispelled a fear that they were caused by a bacterial endocarditis or a rheumatic purpura. Like the Chinaman, do not just look but "look-see," and after seeing well, supplement the general survey by whatever other examinations are needed to prove what ails the sick man. "He will treat the disease properly whom the first origin of the cause has not deceived."

During the period of investigation, be thorough and avoid living by the watch, for haste causes errors of omission more numerous and frequently more serious than are those of commission. In giving advice or information, be deliberate, not hesitant; cheerful, not facetious; understanding, but sympathetic only in so far as this will not be prejudicial to treatment. It is well to give patients who have an acute or a self-limited disease an approximate estimate of when they will recover and when they will be able to resume their usual activities, for such information will be a comfort to them, but with those whose period of illness is, so far as you can say, indeterminate, do not guess. If you state the likely length of incapacity and it proves to be shorter than promised, it may be a gratification, whereas if it be longer than was forecast, there will be disappointment or even depression.

In the hospital and the home, a knack or facility in carrying out what are considered generally to be nursing procedures is often useful; the arrangement of pillows and rolls probably accomplish as much for Rollier in his treatment of tuberculosis of the bones and joints as do the supports and extension used generally by others. Ingenuity in devising and setting a back rest or in placing a binder or sandbag may lessen dyspnea, local pain or cough more effectually than a drug, and unlike the latter, may remove the pain from the patient instead of divorcing the patient from his pain. So, too, if you can fill a prescription for a cook or a nursemaid, supply a hobby for idleness or alter the habits of a member of the household, you may cure the bodily expressions of ineffectual effort, convert a complaining parasite into a cheerful producer, and abort a state of invalidism that was based on unhappiness. Regard a person as an important patient only in so far as he needs your care, and not with relation to his financial or social position. You will find it helpful to appraise the intellectual and the emotional status of the patient and of his household, partly to determine how likely they are to co-operate with you, and partly to judge how best to tell them the facts they should know.

In many cases, to gain the full co-operation of the patient you must tell him exactly the nature or the gravity of his illness. If he has a disease that demands rest, will he abandon his career to secure it when he has been assured that he has no serious physical fault? Put yourself in his place, and consider what your reaction would be if in one breath you were assured that examination showed no reason to consider your pain to be of circulatory origin, and in the next were counseled to withdraw from active practice, to abstain from tobacco, from physical and emotional strain and to take a vasodilating drug. If the patient has a metabolic disorder, will he control his desires unless he is convinced that there is need to? Would you give over your epicurean delights without convincing word that it was necessary to do so?

How best to acquaint anyone with the facts of his condition may be difficult and take both time and finesse, but the reward is worth the effort. Bad tidings need not be imparted brutally, — even in boxing one does not hit below the belt, — and hard facts may be softened with a padding of careful phrasing and still have their import sufficiently clear. Secrecy invites discovery, and if discovery of concealment and falsehood comes, it will break the confidence on which the success or failure of treatment often depends, and replace

it with a fear that may be worse than the truth itself would have been. If a person asks that if you find anything wrong with him you do not tell him, try to make it clear that if you made and kept that pledge he would have no benefit from your opinion, and suggest that he would be wiser to consult someone else.

When a patient is seriously ill and the outlook for him is in doubt, it is justifiable to express the hope that the chances for his recovery are better than they seem to be at the moment, but if he appears to be fatally sick, it is rarely well to indicate to him the impending outcome. There is no rigid rule that will suffice to meet all situations. If possible, and generally it is, the full truth of the situation should be told to some responsible relative or friend, provided he has sufficient intelligence, is physically and emotionally fit to receive it and is sufficiently discreet to hold a confidence. It will be necessary so to judge people as to know whether it is wiser to tell them the truth, the whole truth and nothing but the truth, or to deviate from complete frankness to the extent of deleting that part of the truth the telling of which would leave hope behind. Although generally a partial truth is worse than a lie, incomplete information that is told without distortion of fact and in a way to buffer its full significance will spare avoidable sorrow and even be a source of comfort. There is no more helpful ability in a time of grave crisis than skill — merciful, not Machiavellian — to tell bad tidings with a minimum of hurt to the hearer.

In private practice, patients with functional nervous disorders are perhaps even more numerous than they are in the hospital. An understanding of how to cure these disorders is necessary not only for that primary purpose, but because the same skill is required to deal with the psychic dysfunction that few with organic disease escape. If you learn to deal wisely with the former, you will be better equipped to treat skillfully those with physical ailments. In so far as you study them carefully to exclude latent disease, there will be fewer tokens of your diagnostic limitations, and with reasonable skill you may solve the problem for those who ignorantly but sincerely consider psychiatric care a stigma, recommending the services of a psychiatrist only for those in need of his specialized training. These patients will be your despair or your delight: your despair because of the obscure problems they may present; your delight because cared for properly they will recover and be the leaven of many depressing experiences. They cannot be dispatched toward health with "There is nothing wrong with you."

Here is your medical ticket, use it and your safe journey to Welldom is assured" They need a personally conducted tour initiated by planning and a fund of confidence "Your case is clear I resent for you the inference that your pains are imaginary, you have them but you misinterpret their meaning because of the way your nervous system is working at present I know they are disagreeable, but if you will bear with them they will pass and will leave you unharmed They are not mental, it is your emotions, not your mind, that are upset", such statements make the fund of reassurance for the trip, the road of which is leveled by the removal of inner conflict, of mal adjustments to domestic, social and economic factors, and is smoothed by physical therapy and psychotherapy In such measure as you understand a sick personality, your treatment will succeed or fail This is illustrated as well in the care of the tuberculous as in the treatment of a neurosis uncomplicated by bodily disease The head of a family develops pulmonary tuberculosis Suddenly, the course of his life is changed, to adjust him to his altered status requires more than the direction that he be resigned to an indefinite furlough from active work or that he leave his home for institutional care Friendly, detailed inquiry may indicate that he is disturbed more by unselfish thoughts than by concern for his own well being If his fears for the health of his family are not allayed by careful examination of those who were exposed to his infection, if his anxiety as to how they will get on while he is ill or away is not relieved, if his disappointment and his depression, induced by a gloomy outlook on the future, are not lessened by the acquisition of a better estimate of his condition, he may refuse to accept good therapeutic advice, or if he does accept it, an uneasy mind and nervous tension during the period of enforced invalidism may slow or even prevent his recovery

In interesting contrast to the so called "nervous patients" are those who, although they are neither neurotic nor organically ill, are not quite healthy They may practice moderation in all things, yet they are hampered by fatigue, aches and pains They attempt to do more than their capacity warrants, endeavor to pursue the ways of the vigorous, and unlike psychoneurotic patients, try to ignore their symptoms and struggle to work in spite of them They resent rather than capitalize their physical inadequacy They are legion in practice, and however thoroughly studied show no discoverable disease Not suggestible, well balanced emotionally, occupied constructively, they fall a prey less readily to quackery and to cults than do their

nervous brethren, but they are often the recipients of medicines instead of instructions as to how to live within the range of their physical capacities. Experienced clinicians have noted that these patients must be taught to realize that although their bodies are sound, their reserve is low, that they must be persuaded to curb their ambitions and to limit their activities, and to replace medication with living that although limited can still be useful Their needs are not unlike those who have a chronic local disease in an otherwise fairly sound body Since in these cases the affected part cannot be made normal, a new way of living must be sought, for successful attempts to improve the general condition too much may result in complete disability Nature shows the way when she slows the man who has myocardial disease with an intermittent claudication, when she halts the tuberculous with lessened endurance and the hypertensive with a sense of exhaustion It may be difficult to decide whether the restoration of a sense of efficiency would be useful or only comfortable, and it may be wise to direct such patients in an unorthodox way, or even to foster semi invalidism in order to prolong life

To neither of these groups will you give placebos In fact, the placebo has no place in medicine unless it be given in answer to the cry of an anxious family that some medication be given Prescribed solely to satisfy a patient, such treatment is a therapeutic lie and lays a foundation for mistrust or disillusionment, and is a poor substitute for re-education More than thirty years ago, Doctor Richard Cabot cited an illustrative case to a group of us who were students at the Massachusetts General Hospital A neurotic young woman came to the dispensary complaining that she had a frog in her stomach The diagnostic study showed nothing physically wrong Perhaps pressed for time, lazy or possibly mistrustful of his therapeutic ability, the physician on duty prescribed methylene blue, indicating that the medicine would dissolve the amphibian He told the lady proof of the successful action of the drug would be visible to her—she would void green urine She did and was convinced! But the therapeutic triumph had only a brief day Within a short time the patient returned more distressed than ever. "Doctor, my first frog was a female—she had laid eggs before she was dissolved, and now the tadpoles make me feel worse than their mother did!" Nor could she be convinced that her first gastric tenant was a male!

There are other placebos that though unlabeled are as impotent permanently to help as are sugar

pills and potions. The administration of the newest even if untested remedies to give an impression of being up to date; the assumption of a manner of authority unwarranted by wisdom; the imparting of an idea that what is prescribed is of one's own creation; indulging in boasting, bombast or mystery, are of the same ilk. Sound practice shuns the apparent help of such crass substitutes for skill, and relies on better ways to gain and to stabilize confidence.

All that you do in the way of studying the individual patient has as its ultimate purpose understanding of how best to relieve him of his symptoms, to cure him of his illness, to help him regain and to maintain a state of efficiency. Your aim will not be merely to discover such means but to devise a plan that will be adopted, realizing that success of the regimen will be influenced by your ability to instill hope and the courage to regain health. Your responsibility in doing this will be more individual and direct in private practice than it is in the hospital. It will usually be yours alone to decide what is best to do, when and how to do it, when to stand by to carry out measures, when to remain to give moral support in order to allay fear or give comfort. If you are able to convince relatives that their absence from the sickroom is desirable so that they will forego frequent visits to it, you will save the patient the needless strain of conversation and the effort that many expend to appear better than they really are, and this will be just so much reserve spared to favor recovery. If you can persuade them that their unexpected arrival from another city will be interpreted by the sick one as a sure index of the real or potential gravity of his status, and can dissuade them from the contact with him, it will often be of more benefit than anything else you can do.

You will have to detail directions so clearly that an untrained kinsman or aide can comprehend them sufficiently well to fill them precisely, and if you leave word that you can be reached if needed, that will lessen worry. It may be that you will be inclined to rely on simple measures, the offspring of tested usage and of common sense, supplemented by some well-known medication, the indication for which is clear and the effect of which is to be relied on, but this inclination may be questioned by the opposition of volunteer advisers, for most laymen have their own medical ideas and their own favored remedies. They are sure they have a hereditary aptitude and that they have been schooled well by the press, magazines and radio. Few will be satisfied unless active measures of treatment are instituted, but although

patient and tolerant with them, do not let them lead you into an unwise course. Usually, it will be simple to retain complete direction and to avoid overtreatment, but in times of crisis or impending disaster it will require fortitude to maintain a judicious inaction, to refrain from medical therapy just to be doing something. At such a time, to protect the patient from heroic treatments, from an operation of adventure rather than one of exploration, may court an indictment of incompetence, and to shield your charge from the worry and fatigue of examinations by an army of consultants may bring a criticism of self-protection or of vanity. In such case it will often profit much to explain patiently and clearly the reasons why suggested measures are not taken, why doing so would be more hurtful than beneficial; to indicate that the failure to be aggressive is based not on failure to think of utilizing this or that procedure, but on a considered rejection of them at a given time; and to reinforce your decision by helpful consultation. By such means confidence can be restored and your less divided attention can be given to the immediate care of the patient. Uninfluenced by the tide of fashion, use measures as simple and as inexpensive as possible without sacrifice of merit, but be ready to employ new remedies if you have the means available to control their action. Avoid administration by injection when the giving by mouth is as effectual, an injunction particularly timely when the urge to inject intravenously seems to be needlessly general, and withhold any other heralded remedy unless the need for it is established. Endeavor generally to utilize accepted drugs, notwithstanding the enthusiastic claim made for the superiority of proprietary preparations or for standard chemicals with a trade name, if only to save wasteful expenditure. Be informed of therapeutic advances, and although quick to adopt new measures as promptly as their worth has been established, avoid the prescription of those which have only novelty to commend them. The trust that something can be given to drive out the demon Disease lingers now as always, and has only been translated from a wishful faith in the ointment of Haldanus, in the sympathetic powder of Digby or in Perkins's tractors, to a scarcely less rational confidence in infusions, transfusions, new drugs and popularisms. Neither unsupported claims nor the tide of fashion can challenge successfully the truth of Osler's statement that drugs are the most uncertain element in our art, nor of Benjamin Franklin's appraisal of the wise doctor as "he who knows the worthlessness of most medicines."

The protective function of the doctor gives him many problems, of which by no means the least is to determine to what extent he should employ heroic or expensive measures that frequently cause disagreeable or even dangerous symptoms, and that can only postpone briefly the fatal ending of a hopeless illness.

A man of fifty-four, with a myelosis so advanced that it had caused destruction of many ribs and involved the spine so extensively as to necessitate a completely bedridden state for twenty months, developed a pneumococcal pneumonia. Was there justification for administering sulfur pyridine, that would probably have caused distressing nausea and vomiting, perhaps a painful renal colic, and made him suffer vainly and perhaps robbed him of any easy passing piloted by "the old man's friend"? And a lad of seventeen, all but moribund with a classic acute leukemia should he not have been spared repeated transfusions, that at best could have done no more than to prolong his existence for a few brief days, and thus have lessened the financial stress of his family? In such surely fatal diseases there can be only one dictum: face reality, relieve suffering and await the closing hours. This is not to countenance euthanasia, for so long as medical knowledge is limited and prognostic judgment fallible, you will use all legitimate means to maintain life whenever there is a reasonable expectation that an adjusted living may follow the immediate crisis. Oliver Wendell Holmes indicated as much when he referred to man's unwillingness to exchange the mixture of nitrogen and oxygen called air for any other atmosphere, however light to breathe.

Rest, diet and a change of residence for the sake of health should be modified to meet individual needs. Although rest in bed is essential, even imperative at times, it will be really beneficial only if it includes a comfortable bed, competent nursing care, mental calm and the visits only of those whose brief stay may bring ease or cheer. Now and again it may fail of its purpose, unless your ingenuity and cleverness are sufficient to provide equally restful conditions on couch or chair, or to devise ways to occupy or to divert during the time of physical restriction. In the same way, the full benefits of climatic treatment are derivable only if the patient's choice of location and his reactions to altitude and to temperature are considered. One man sent to Saranac Lake feels banished to Siberia; another delights in the winter cold. One bidden to the desert will languish there, another flourish; and a change of residence made to regain or to maintain health may lose

its potential value unless it weighs also the effects of the disruption of familial, social and economic ties. In planning the dietary of patients you may treat for conditions other than metabolic or allergic diseases that require definite restriction of or additions to the menu, a thoughtfully supervised choice of food often offers a way to overcome lack of appetite, to shorten convalescence and to give pleasure. Rigid ideas concerning the digestibility of any article of diet are not justified. What makes your psychic secretion flow may inhibit mine. What causes pain to one gives comfort to another. The food that distends "her" may leave "his" belt relaxed, and what binds Mary may purge John. Truly, one man's food may be another's poison, and if you fear the challenge of being unscientific, if you permit a person's taste to help determine what he shall eat, remember Richter's experiments, which demonstrated that the craving for a particular food can be caused by physiologic needs.

In order to complete the care of a sick person, it is your obligation to guide him through the time of convalescence until he has been restored not only to well being but to normal living. Healed but not recovered, if he is deserted professionally before he is well, he may suffer needlessly or even relapse, whereas the supervised resumption of physical and of mental activity so gradually that they prevent fatigue, the provision of fresh air and of sunshine, of wholesome tempting food, of a little wine or a smoke and good company, would ensure and hasten a happy restoration of well being.

Finally, the care of the sick includes the teaching of a way of life that is lived in accordance with the rules of hygiene in the fullest sense. If you are charged with the care of a patient who has a hereditary, a familial or a contagious disease, it is your direct obligation to teach him all known measures to prevent its transmission to others, and thus with his co-operation to endeavor to lessen the incidence of sickness and disability. This duty of preventing disease has happily received increasing attention in recent years, but it is unfulfilled at times because of carelessness, or is slighted because of the obstinacy or the selfishness of the patient. In one case, he may insist that his contemplated unwise mating menaces none in an era in which ways to prevent parenthood are accessible and reliable, and in another it may be difficult to convince him that his tuberculosis is contagious, his syphilis is communicable, his acute respiratory infection is a menace to those about him, although he is ready to recognize the hazards that another's consumption, another's pox or another's cold offers to his

fellows. In so far as each physician undertakes correctly to direct each of his patients, the incidence of disease will be lessened and the unhappy emotional upsets due to proper self-incrimination that follow disregard of sound eugenic and hygienic measures will be averted.

So on and on, the review of the essentials of the proper care of the sick might be narrated and stressed, but perhaps enough has been said to indicate the functions of him who ministers to the patient. In essence, they are to in-

dividualize the patient; to treat him rather than his disease; to protect him from misguided direction; to guide him and his family in a way that will bring a good adjustment to a temporarily or a permanently altered status, with a minimum of emotional and of economic strain and that will restore a well-ordered way of life. As Trudeau is quoted to have often said, "To cure sometimes, to relieve often, to comfort always"—that is the job of the doctor.

1417 Eutaw Place

THE DIAGNOSIS OF MARIE-STRÜMPPELL ARTHRITIS WITH CERTAIN ASPECTS OF TREATMENT*

HUGH F. HARE, M.D.†

BOSTON

MARIE-STRÜMPPELL arthritis is a painful, crippling disease producing stiffening and rigidity of the spine of young persons. It is a slowly progressive, incapacitating condition, leading to complete bony ankylosis of the vertebral column and to invalidism.

It is estimated that there are 6000 invalids from various types of arthritis in Massachusetts. What proportion of them are incapacitated by Marie-Strümpell arthritis cannot be easily estimated, since there is no attempt at present to segregate the various forms. During a two-year period at the Lahey Clinic we have observed 1179 cases of arthritis, 357 of which were of the rheumatoid type. Of these, 21 (6 per cent) were of the Marie-Strümpell type. This paper is a further report of these patients, who have been under observation and x-ray treatment for at least a year. A preliminary report¹ was published in April, 1940.

The etiology of this condition is unknown. Presumably it is a form of rheumatoid arthritis usually originating in the sacroiliac articulations, and accompanied or followed by inflammation of the apophyseal joints. The inflammatory state may last from weeks to years, the joints gradually becoming stiffened. Associated with the inflammatory changes in the vertebral facets or apophyseal joints, calcification of the spinal ligaments may occur either in all these structures or in localized portions of one or more. When calcification of the spinal ligaments is complete, one sees the classic roentgenograms of the "bamboo" spine. It is a disease of young adults, the symptoms starting between the ages of twenty and twenty-five

years. It is ten times more frequent in men than in women, a reversal of the sex ratio noted in other forms of rheumatoid arthritis. In this series the diagnosis was not made until the average age of thirty, showing a lapse of years between the first symptoms and the correct diagnosis.

The disease may be arbitrarily divided into three phases. In the early stage a bizarre clinical syndrome is presented, characterized by shifting pains of a rheumatic nature in the limbs, chest and peripheral joints. The pains may last for several days or weeks, then disappear for several months or years. This period is known as the pre-spondylitic phase. The process may become inactive at this time; if so, it leaves no physical handicaps. If the disease is progressive, the pain shifts to the low-back or sacroiliac region, and is said to be in the "sacroiliitis" phase. During this period the patient is frequently able to carry on his daily work, because the discomfort is more marked at night, several hours after retiring. Many patients, when awakened at night by backache, obtain relief by getting up and moving about, by taking aspirin or by being massaged. Stiffness in the early morning, which disappears following exercise, is common. Pain is often brought on by stubbing the toes or by jarring heavily on the heels when walking downstairs.

As the disease progresses, pain is present along the entire spine, associated with stiffness and eventually rigidity, producing the classic "poker-back" deformity. Occasionally there may be involvement of peripheral joints in the latter stage.

The physical findings depend on the phase of the disease. During the pre-spondylitic stage, that is,

*Department of Radiology, the Lahey Clinic.

†Radiologist, Lahey Clinic.

during the period of wandering pain, physical examination is essentially negative. In the phase of sacroiliitis there is increasing pain and tenderness along the course of the spine, limitation of motion, muscle wasting and decrease in chest expansion and vital capacity. It has been shown that pain and spasm are outstanding causes of limitation of motion, but once calcification takes place in the ligamentous structures, rigidity is complete. The most frequent deformity is dorsal bowing, with rigidity of the neck, which makes the patient carry the head in front of the body. In only 4 cases was there involvement of the peripheral joints.

Foci of infection have been searched for; they have been removed whenever possible.

A finding common in all cases during activity is an increased sedimentation rate. One patient in the series had associated diarrhea, and studies of the stool revealed idiopathic steatorrhea. Other laboratory findings have been consistently negative.

The reports of Scott,² Golding³ and Forestier⁴ showed that bony involvement is frequently first apparent in the sacroiliac articulation, and that only rarely is the disease present without such involvement. Study of the present series of cases confirms their findings.

Roentgen-ray diagnosis during the early or prespondylitic stage of the disease is not possible, since there are no demonstrable bone or ligamentous changes. During the phase of sacroiliitis, however, definite bony changes may involve the sacroiliac articulations, consisting of symmetrical changes of the sacroiliac region, wherein there is increased density or osteosclerotic reaction surrounding the joint, with slight narrowing of the joint spaces. In order to bring out slight bony changes in the sacroiliac joints, it is necessary to take roentgenograms of this region with the sacrum in a longitudinal axis. This projection is commonly known as the 15°-angle view and is taken with the patient in the supine position with knees flexed and with the x-ray tube tilted 15° cephalad. This projection allows a view of the sacroiliac joints without distortion.

As the disease progresses changes gradually become apparent around the apophyseal joints or articulating facets, the joint spaces appearing narrowed or obliterated. Decalcification of the body of the vertebrae may be noted, probably due to atrophy of disuse. Still later, calcification of the ligaments may be observed. Gradually the entire spine appears to be fitted with a calcified casing partially obliterating the individual bony struc-

tures. This is known as the "bamboo" spine. Ligamentous calcification is differentiated from hypertrophic degenerative lesions by the lack of osteophytes in the former condition, and by location; degenerative spurs arise from the margins of the vertebrae and are contiguous with them, whereas ligamentous calcification appears to arise from the bodies of the vertebrae. All ligaments of the spine may be involved, including the ligamenta flava.

The differential diagnosis should not be difficult with the aid of roentgenograms. The lesions which may be confused most frequently with this condition are those of degenerative arthritis, metastatic cancer, Paget's disease and other types of rheumatoid arthritis.

During the last three years we at the Lahey Clinic have become more conscious of this disease, both clinically and roentgenologically, than previously, and have diagnosed more than 35 cases during this period. This is a larger group than had ever been diagnosed in the clinic prior to this time.

Radiation therapy was first described by Scott,² who reported on the successful treatment of over 150 cases in which follow-up studies were made for a period of three to five years. This treatment gave relief of pain and decreased the amount of stiffness that the patient presented. In cases in which the disease had progressed to calcification of the ligaments and obliteration of the apophyseal joints, clinical improvement occurred, but there were no roentgenologic changes to show decrease in the ligamentous calcification or changes in the sacroiliac or apophyseal joints.

It is difficult at best to evaluate therapy of this condition because of spontaneous remissions and exacerbations of the disease, because the disease may become inactive at any time, and because it progresses so slowly that one must depend on clinical findings and objective improvement.

Treatment consists of relieving pain and preventing deformities. Since there is no specific treatment of this condition, various methods have been used to relieve pain and to prevent and correct deformities.

Bed rest with the spine held in extension has been widely used. This procedure has been successful in relieving pain and preventing and correcting deformities, but because the disease is slowly progressive, continuing over a period of years, bed rest must be carried out over a long period during which there is gradual muscle-wasting, and rehabilitation of the patient to make him a useful citizen is a long-drawn-out process.

Case No.	Age	Sex	Duration of Symp- toms	Time Obs- erved After Treat- ment	No. of X-Ray Treat- ments	Involvement	Sedimentation Rate		Vital Capacity		Chest Expansion		Weight		Foci of Chronic Infection	Symptoms and Findings	Results
							Before	After	Before	After	Before	After	Before	After			
1	yr. 24	M	4	20	12	Sacroiliac joints	mm. 1.90	mm. 1.40	cc. 3000	cc. 3800	in. 1½	in. 2¼	lb. 144	lb. 188	Tonsils	Pain + + + + Stiffness + + + + Limitation + + + +	Pain 0 Stiffness + + Limitation + +
2	31	M	11	13	10	Sacroiliac joints Lumbar spines Dorsal spines	0.60	0.75	1800	3000	½	1	171	185	Tonsils	Pain + + + + Stiffness + + + + Limitation + + + +	Pain 0 Stiffness + + Limitation + +
3	42	M	12	9	6	Sacroiliac joints Lumbar spines Dorsal spines	0.84		1600	2400	½	2½	178	175	Sinuses	Pain + + + + Stiffness + + + + Limitation + + + +	Pain + + + + Stiffness + + + + Limitation + + + +
4	23	M	3	14	15	Sacroiliac joints	0.95	0.91	2300	2600	1½	2½	123	127	None	Pain + + + + Stiffness + + + + Limitation + + + +	Pain + + + + Stiffness + + + + Limitation + + + +
5	33	M	5	12	9	Sacroiliac joints Lumbar spines Dorsal spines	1.39		2000	2100	½	1	100	117	Tonsils	Pain + + + + Stiffness + + + + Limitation + + + +	Pain 0 Stiffness + + Limitation + +
6	21	M	4	12	12	Sacroiliac joints	0.72	0.54	2300	2900	½	2½	113	116	Tonsils	Pain + + + + Stiffness + + + + Limitation + + + +	Pain 0 Stiffness + + Limitation + +
7	28	M	4	12	8	Sacroiliac joints Cervical spines	1.19	0.74	2500	2900	½	1	162	165	None	Pain + + + + Stiffness + + + + Limitation + + + +	Pain 0 Stiffness + + Limitation + +
8	30	M	8	11	7	Sacroiliac joints	0.20		4600	4800	2	2½	160	164	None	Pain + + + + Stiffness + + + + Limitation + + + +	Pain 0 Stiffness + + Limitation + +
9	34	M	1	9	7	Sacroiliac joints Dorsal spines	1.20		2300	2500	1	1	161	156	Tonsils	Pain + + + + Stiffness + + + + Limitation + + + +	Pain 0 Stiffness + + Limitation + +
10	27	F	7	9	5	Sacroiliac joints Lumbar spines Dorsal spines	0.72		2000	2000	1¼	1½	132	132	None	Pain + + + + Stiffness + + + + Limitation + + + +	Pain 0 Stiffness + + Limitation + +
11	33	M	1	10	6	Sacroiliac joints	0.36		4000		2		151		None	Pain + + + + Stiffness + + + + Limitation + + + +	Pain + + + + Stiffness + + + + Limitation + + + +
12	27	M	4	12	3	Sacroiliac joints Dorsal spines	0.11		3600	3500	2½		147		None	Pain + + + + Stiffness + + + + Limitation + + + +	Pain + + + + Stiffness + + + + Limitation + + + +
13	24	M	4	4		Sacroiliac joints	0.52		5000	5000	3	3	152	162	None	Pain + + + + Stiffness + + + + Limitation + + + +	Pain + + + + Stiffness + + + + Limitation + + + +
14	44	M	20	4		Entire spine Knees	1.10		2800	2800	1½	1½	138	140	Tonsils	Pain + + + + Stiffness + + + + Limitation + + + +	Pain 0 Stiffness + + + + Limitation + + + +
15	25	M	2	12		Sacroiliac joints	0.28		5000	5000	3	3	165		Sinuses	Pain + + + + Stiffness + + + + Limitation + + + +	Pain + + + + Stiffness + + + + Limitation + + + +
16	26	M	4	5		Sacroiliac joints	0.80		3150	3500	1½	1½	153	162	Tonsils	Pain + + + + Stiffness + + + + Limitation + + + +	Pain 0 Stiffness + + + + Limitation + + + +
17	29	M	12	4		Sacroiliac joints Spine	0.34		2300	2400			103	110	None	Pain + + + + Stiffness + + + + Limitation + + + +	Pain + + + + Stiffness + + + + Limitation + + + +
18	39	M	1½	7		Sacroiliac joints Spine	1.26		1500	1800	½	1½	127	121	None	Pain + + + + Stiffness + + + + Limitation + + + +	Pain 0 Stiffness + + + + Limitation + + + +
19	34	M	5	4		Sacroiliac joints	0.38		3000	3300	1¼	2½	137	141	None	Pain + + + + Stiffness + + + + Limitation + + + +	Pain + + + + Stiffness + + + + Limitation + + + +
20	32	F	5	10		Sacroiliac joints Spine	0.96	1.15	1800		1		116		None	Pain + + + + Stiffness + + + + Limitation + + + +	Pain + + + + Stiffness + + + + Limitation + + + +

A modification of the above procedure, now advocated by Swaim,⁶ consists of putting the patient to bed until relief is obtained, and then giving him a form-fitting jacket to wear. This has been successful in preventing deformities and, according to Swaim, largely relieves pain and prevents involvement of the peripheral joints.

Forestier⁴ reports the successful use of intramuscular injections of gold salt and of weekly intramuscular injections of radon.

It has been my impression after treating a series of 35 patients with x-rays that relief of pain can be obtained in about 80 per cent of cases. The maximal number of treatments given to any one patient has been twenty. A patient whose course has been followed for two years received no treatment during the last year and has remained free of discomfort. Roentgen examination two years after the first treatment revealed progression of the disease evidenced by calcified bridging in the ligaments of the low lumbar spine. Probably the best test of the value of radiation treatment has been that 33 of the 35 patients are now able to work; this includes 5 patients who were formerly incapacitated. Nineteen of the 21 patients observed within a year have also returned to work.

Radiation therapy is directed to the entire spine, the sacroiliac joints, and the paravertebral and gluteal muscles. Only small doses of x-rays are required to give relief. At present I am using six portals of 300 sq. cm. each, treating one portal daily; a dose of 300 r is administered to each portal, using the following factors: 150-200 kv.; 20 milliamp.; filters, 0.25 to 0.5 mm. of copper and 1 mm. of aluminum; distance, 50 cm. (In the 2 young women whom I have treated, a maximum of 100 r has been used over the low-lumbar and sacroiliac regions in order not to injure the ovaries.) This series may be repeated again in three weeks if necessary, although usually only one or two areas will require further treatment, depending largely on the stage of the disease at the time treatment is undertaken.

Relief of pain may be noted during the first week, or two or three weeks following radiation treatment. In some cases it has been necessary to repeat the series in order to obtain relief. If occasional attacks of pain recur, they may usually be relieved by a single small dose of x-rays.

When relief of pain has been obtained it is advisable to refer the patient to the orthopedic sur-

geon for muscle-building exercises and for correction of the deformities that have already taken place. Muscle-rebuilding has been slow; only 2 patients in this series have returned to hard manual labor. The use of back braces or supports following radiation therapy has not been necessary.

SUMMARY

The etiology of Marie-Strümpell arthritis is unknown. It is a disease of young adults; it is ten times more frequent in men than in women. The disease produces painful, progressive rigidity of the spine.

The clinical findings are pain, stiffness and limitation of motion of the spine.

Elevation of the sedimentation rate is a constant factor.

The diagnosis of this disease before rigidity of the spine has taken place may be made by roentgenograms, since the disease attacks the sacroiliac joints apparently before other portions of the spine, producing symmetrical changes of increased density and narrowing of the joints before calcification occurs in the ligaments.

Radiation therapy directed over the spine and the sacroiliac region will in most cases relieve pain and thereby prevent deformities, although the disease may continue to progress.

This condition varies from the usual form of arthritis in several ways:

It is a disease of young men, usually of the athletic type, a reversal of the usual sex ratio as compared with other types of rheumatoid arthritis.

Peripheral-joint involvement is infrequent.

Pathologic changes first appear in the sacroiliac articulations.

Calcification in ligaments, which does not occur in other forms of rheumatoid arthritis, is always present in the late stages.

Relief of pain is obtained by x-ray treatment.

REFERENCES

1. Hare, H. F., and Kimmel, C. B.: Treatment of atrophic spondylitis with radiation therapy. Preliminary report. *Lancet Clin. Bull.* 1 (No. 7) 22-26, 1940.
2. Scott, S. G.: Chronic infection of sacro-iliac joints as possible cause of spondylitis ankylosans. *Brit. J. Radiol.* 9:126-131, 1916. Radiology and the rheumatic backache. *J. Roy. Inst. Pub. Health & Hyg.* 12:236-244, 1938.
3. Golding, F. C.: Spondylitis ankylopoietica (spondylitis ossificans ligamentosa). *Brit. J. Surg.* 23:484-500, 1936.
4. Forestier, J.: Importance of sacro-iliac changes in early diagnosis of ankylosing spondylitis: Marie-Strümpell-Recherew disease. *Radiology* 33:389-402, 1939.
5. Swaim, L. T.: Orthopaedic treatment of Strümpell-Marie arthritis. *J. Bone & Joint Surg.* 21:983-991, 1939.

TUBERCULOUS TENOSYNOVITIS

RALPH ADAMS, M.D.,* GORDON JONES, M.D.,† AND HENRY C. MARBLE, M.D.‡

BOSTON

CASES of tuberculous tenosynovitis have been but rarely seen at the Massachusetts General Hospital during the last half-century. Thirty-six cases of the disease were found in a survey covering the last forty-five years. A disease which is seen only once in every 7891 admissions to a large metropolitan general hospital merits recurrent analysis, even though several excellent descriptions are extant.

The age decade most commonly affected is the third, but there is a wide age distribution. This is shown in Figure 1. The youngest patient was

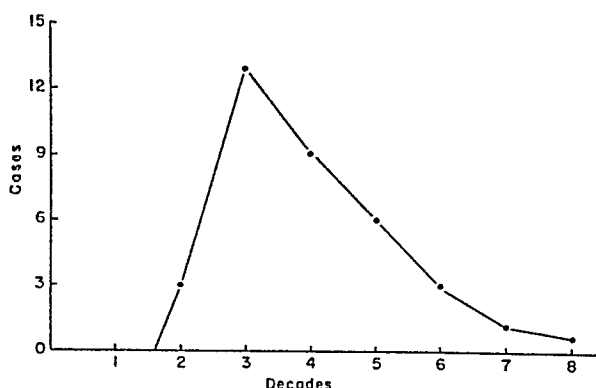


FIGURE 1.

fifteen years old, with symptoms of one and a half year's duration, and the oldest was seventy-five, with symptoms of three years' duration when first seen. The average age was thirty-six years. The median age was 33.5 years. There were 21 males and 15 females.

The right hand was involved in 22 cases: on the volar surface in 15, the dorsal surface in 6 and both surfaces in 1. Five of these patients were right-handed, 1 was left-handed, and in 16 cases no record was made. The left hand was involved in 14 cases: on the volar surface in 8, the dorsal surface in 5 and both surfaces in 1. One of these patients was right-handed, 2 were left-handed, and in 11 cases no record was made. Stated differently, the volar surface was involved twenty-five times, and the dorsal surface thirteen times. The influence of use on incidence is shown by the high occurrence of involvement in the right hand of right-

handed patients, and by the fact that most people are right-handed.

The occupations varied widely. There were no laborers, but 30 patients made hard use of their hands. The others included 2 school children, 2 chauffeurs, 1 waiter and 1 fruit dealer. The influence of occupation is inconclusive, but hard use of the hand may be a predisposing factor.

The importance of a history of trauma is difficult to determine. Mild injuries to the hands of working people are so common and hand tuberculosis so rare that attempts at correlation are dangerous. Eight of the patients in this series complained of definite antecedent trauma.

The role of direct inoculation has often been mentioned. The present series furnishes little evidence in support of this method of infection. On the other hand, the reduced incidence in butchers with the decline of bovine tuberculosis and the tightening of pure food laws points to the possibility of direct inoculation. Two of the patients in this series were farmers, who milked cows regularly, and 1 was a skinner in the days before effective bovine control.

It is said that attendants of tuberculous patients are more susceptible than others to the disease, but there has been no case among the attendants of the Rutland State Sanatorium, one of the oldest tuberculosis institutions in the country.

Thirteen of the patients had tuberculosis elsewhere in the body. The lungs were involved four times, the neck twice, the intestines once, the bones of the hand once, the spine twice, the elbow twice and the bones of the foot once. Kanavel¹ has stated that tuberculosis of the tendon sheaths is a not uncommon complication of pulmonary tuberculosis. However, Dufault² reviewed the complete records of the Rutland State Sanatorium and was able to find only 2 cases. That the disease is frequently present without pulmonary infection is certain. There is no case in this series in which tuberculosis became generalized by extension from the tendon sheaths.

Diagnosis in the early stages may be difficult. The typical feature is a gradually developing, painless or slightly tender mass on the volar aspect of the hand. There is partial stiffness with inability completely to flex or to extend the fingers. Diminished strength on grasping is a common com-

*Assistant in surgery, Harvard Medical School; assistant in surgery, Massachusetts General Hospital.

†Assistant resident in orthopedic surgery, Massachusetts General Hospital.

‡Assistant visiting surgeon, Massachusetts General Hospital.

plaint. The presence of disease beneath the carpal ligament may cause mechanical pressure on the median nerve, with paresthesia over its peripheral distribution. One of the most valuable aids in making a diagnosis is the keeping of a four-hour temperature chart over a period of several days. A daily rise in temperature to 99.6 or 100.6°F. is suggestive of tuberculosis and should lead to further study. Suspected cases should of course be splinted from the beginning.

Finger motion may cause creaking or grating sounds in the later stages of the disease, because of the accumulation of degenerated fibrinous deposits within the tendon sheath—so-called "rice bodies." Rice bodies and two-way fluctuation beneath the annular ligament usually mean a burned-out lesion. Joint stiffness and a fluctuant mass often indicate bone disease, which may be proved by x-ray demonstration of destruction of the carpus.

The diagnosis was proved pathologically in 27 of the cases and established beyond a reasonable clinical doubt in the remaining 9. The diagnosis of tuberculous tenosynovitis in this hospital for the past forty-five years has been equivalent to the recommendation of operation; this is proved by the fact that 33 of the 36 patients were so treated. Only two types of operation were performed: incision and drainage of fluctuant masses in 9 cases, and resection of the involved tendon sheaths in 24. Thickened, granular, grayish sheaths, filled with fibrinous concretions (rice bodies), gelatinous material and edematous granulation tissue, are characteristic. In some cases, however, prolonged study of the pathologic material proved necessary before a positive diagnosis of tuberculosis could be established. Guinea-pig inoculation was sometimes helpful.

Follow-up notes are available in 26 of the 36 cases, and in 23 of the 33 operated cases. Six of the latter had drainage procedures, 2 with curettage; 4 failed to improve, 1 was improved, and 1 had repeated small incisions and drainage for three years, with a perfect result at the end of five years. Seventeen patients had excision of the tendon sheaths; 7 were clinically cured. The shortest follow-up period was one year, and the longest sixteen years. The 10 patients in whom arrest failed to be secured by excision continued to suffer from the disease. Seven had relief of symptoms and were clinically improved after operation, although active disease persisted; the others were unimproved or worse as a result of operation.

Two of the 3 patients who were not operated on recovered completely and resumed their work.

The third is unimproved and suffers also from pulmonary tuberculosis.

The results in the 23 operated cases in relation to the duration of disease at the time of operation are shown in Table 1. It should be noted that the

TABLE 1. Results in 23 Operated Cases.

DURATION OF DISEASE AT TIME OF OPERATION	UNIMPROVED CASES	IMPROVED CASES	ARRESTED CASES
yr.			
1 or less	3	0	0
2	0	3	5
3	1	3	0
4	0	2	2
4 and over	3	0	1
Totals	7	8	8

best results were obtained when operation was performed during the second or third year of the disease.

DISCUSSION

These results are none too good. It is striking that tuberculosis, a disease often considered a contraindication to necessary surgical procedures, should have been so avidly attacked when manifested in the tendon sheaths. No other tuberculous condition, with the possible exception of tuberculous lymph nodes of the neck, has been subjected to surgery with such casualness and lack of accessory data.

As is well known, tuberculosis is a generalized disease, and any clinically recognized focus is likely to be paralleled by similar infection elsewhere in the body. A thorough search for such foci is mandatory to the careful clinician. The treatment of tuberculosis of one organ without even awareness of its presence in other organs is obviously a futile procedure.

Furthermore, tuberculosis of the tendon sheaths should receive the same systemic treatment accorded to tuberculosis of the lungs or spine.³ Thoracic surgeons have learned well the value of preliminary sanatorium care; in fact, it is impossible for a tuberculous patient to enter the Massachusetts General Hospital for thoracoplasty unless he has already followed a sanatorium type of regimen. This policy was engendered by many early failures, and remarkably better results have proved its wisdom.

From another viewpoint, surgical attack on a tuberculous focus such as a tendon sheath without knowledge of how the lesion is progressing involves the likelihood of operating in the presence of advancing or exudative disease. This may result in a failure for the surgeon and increased disability for the patient. Knowledge of progression or regression can be gained only by periodic observation, and during this time treatment in the form of splint immobilization and sanatorium type of care should be given.

Again, it is axiomatic that the tuberculous patient must demonstrate resistance and an ability to localize infection before surgical attack is directed on a focal lesion. Attempts at extirpation under other circumstances constitute meddlesome surgery. The fundamental principles governing the treatment of tuberculosis must be followed in tuberculosis of the tendon sheaths as elsewhere,* else the response will be dissemination of the disease.

The drainage procedures which may prove necessary for abscesses about the hand, in order to relieve mechanical pressure, often bring relief of symptoms, but rarely result in arrest of the disease, because the active focus remains. Kanavel¹ has stated that complete removal of tuberculous tendon sheaths or tuberculous tendons will effect a cure. He insisted that every vestige of tuberculous tissue must be removed. If true, this means that one must wait before performing excision until the exudative phase is over and the fibrotic phase is well under way. The task is certainly impossible at any earlier stage. The judgment of this master of the hand was undoubtedly reflected in his ability to select the proper time for operation.

*Renal tuberculosis is to some extent an exception, in that it does not tend to undergo encapsulation and regression.

The best surgical results at the Massachusetts General Hospital have been obtained in cases where the hand has been disabled by the sequelae of an infection that has become quiescent, that is, by fibrosis of tendon sheaths, adherent tendons and rice bodies. Six of the 10 arrested cases were of this type.

Too few of these cases received conservative rest treatment to permit statistical analysis. There is every reason to believe, however, that this form of therapy should more commonly be the primary part of the therapeutic program.

SUMMARY

The diagnostic features and results of treatment for all cases of tuberculous tenosynovitis encountered during the past forty-seven years in a large general hospital are analyzed.

Some principles of tuberculosis therapy are discussed, as specifically applicable to tendon-sheath disease.

REFERENCES

1. Kanavel, A. B.: Tuberculous tenosynovitis of the hand. *Surg., Gynec. & Obst.* 37:635-647, 1923.
2. Dufault, P.: personal communication.
3. Mason, M. L.: Tuberculous tenosynovitis of the hand: a study of thirty-three cases of chronic tenosynovitis of the hand. *Surg., Gynec. & Obst.* 59:363-396, 1934.

CLINICAL AND ELECTROENCEPHALOGRAPHIC CHANGES PRODUCED BY A SENSITIVE CAROTID SINUS OF THE CEREBRAL TYPE*

JOHN ROMANO, M.D.,† EUGENE A. STEAD, JR., M.D.,† AND Z. EILEEN TAYLOR, M.D.‡

BOSTON

UNCONSCIOUSNESS produced by the direct effect of afferent impulses from the carotid sinus on the brain was first reported by Weiss and Baker¹ and its mechanisms first studied by Ferris, Capps and Weiss.² These authors reported that in certain subjects syncope was produced by pressure on the carotid sinus, without changes in heart rate or blood pressure and with no demonstrable decrease in cerebral blood flow. They called this the cerebral type of carotid-sinus response, and believed that the afferent impulses affected certain centers in the brain, or produced local changes in the circulation of these centers, in such a way that unconsciousness resulted.

In many cases it is difficult to determine whether the syncope is due to a sensitive carotid sinus of the cerebral type or is of psychogenic origin. Therefore, a subject was studied in whom attacks were produced by external pressure on the sensitive carotid sinus, by stimulation of the carotid sinus through the intravenous injection of sodium cyanide, and by hyperventilation. Electroencephalograms were taken at rest and during attacks induced by each of the three methods. The sensitive carotid sinus was novocainized, and the procedures were repeated. An operation was then performed in which the right carotid sinus was denervated, and subsequent to this, electroencephalograms were repeated at rest, following the injection of cyanide and during hyperventilation.

*From the Medical Clinic, Peter Bent Brigham Hospital, and the Department of Medicine, Harvard Medical School.

†Instructor in medicine, Harvard Medical School, associate in medicine, Peter Bent Brigham Hospital.

‡Visiting physician, New England Hospital for Women and Children.

CASE REPORT

The patient, a 36-year-old female hospital attendant, was admitted to the Peter Bent Brigham Hospital on November 10, 1939, complaining of fainting spells and migraine. Her mother and a maternal aunt had experienced fainting spells; another aunt had had migraine. From the age of 12 the patient had had attacks of migraine with typical scotomas, paresthesias of the right hand, arm, shoulder and face, thickness of the tongue and unilateral headache. These symptoms recurred every four to eight weeks for a number of years, but more recently they had occurred irregularly.

At the age of ten the patient had fainting spells in school, lasting for a few minutes and characterized by weakness, light-headedness and mental confusion. There were no tonic or clonic components. She had 6 to 8 attacks in the year following onset. They recurred at the age of 22 and were characterized by sensations of heat, pain and expansion of the right side of the head; the patient felt faint, slumped to the floor and was confused. With recovery from the spells the patient experienced sensations of heat and cold all over the body, without sweating. The confusion lasted from a few minutes to several hours, usually accompanied by anxiety and apprehension. These episodes recurred at irregular intervals. At the age of 24, during pregnancy, she experienced one attack every 7 to 10 days. In the following year she had one attack, and when 28 she had a series of them. No more occurred until she reached the age of 36, when their character changed. In addition to the symptoms previously noted there was numbness of the right side of the face and neck, fullness of the neck, hoarseness and stridor. During three months there were 2 attacks, the latter of which necessitated her admission to the hospital where the attacks increased in frequency to as many as 5 in a day.

Most of the seizures occurred in the daytime. There was no relation to meals or to posture. On a few occasions the patient awoke feeling dyspneic, confused and with a sensation of numbness, pain and heat over the right side of the face.

In addition, the patient always had poor postural adaptation. She became weak and dizzy if she stood for long periods of time, and had postural fainting on a few occasions. While in the upright position she frequently noticed palpitation.

Physical, neurological and laboratory examinations revealed no significant findings. The blood pressure was 100/70. The fasting blood sugar on four occasions ranged from 70 to 85 mg per 100 cc. The heart was normal. There was no evidence of arteriosclerosis. The neck was supple and free of any masses or scars. The right carotid bulb was larger than the left. Pressure over the right carotid sinus produced attacks similar in character to those occurring spontaneously, although of shorter duration. Pressure on the left carotid sinus at times produced a sensation of weakness.

After a series of investigative procedures had been carried out the right carotid bulb was denervated surgically by Dr Elliott C. Cutler on December 5. The arteries were separated from the surrounding sheath and the outer coat was blown away with salt solution introduced through a fine needle. The adventitia was then divided longitudinally and peeled off on both sides. The common carotid artery was denuded of its outer coat for 3 cm below the bifurcation. Both external and internal carotid arteries were denuded of their outer coats for 2 cm above the bifurcation. Great care was taken to remove completely the outer coats in the crotch at the bifurcation. Since op-

eration the patient has been entirely well and pressure on the right carotid sinus has produced no attacks. She was last seen on October 9, 1940.

INVESTIGATIONS

Effect of External Pressure on the Right Carotid Sinus

Firm pressure on the right carotid bulb caused the patient's head to fall back limply. Her face became pale, the voice husky, and she developed stridor. At times, further pressure produced loss of consciousness, tremor in the right hand and twitching of the muscles of the right side of the face. After release of the pressure the patient remained confused for about a minute. The attacks usually occurred without a fall in blood pressure or a change in heart rate. After novocainization, and after surgical denervation, external pressure on the right carotid bulb produced no symptoms or signs of attack.

Effect of Intravenous Injection of Sodium Cyanide

Sodium cyanide is known to stimulate the chemoreceptors in the carotid sinus.³ An injection of 0.04 cc of a 2 per cent solution of sodium cyanide was made into the left antecubital vein, with the left hand immersed in water at 39°C. Injections of physiological salt solution were used for controls. Since the needle was left in the vein during the entire procedure, the patient did not know what was injected or when the injection took place. She had previously been given intravenous saline injections, which had produced no symptoms. Fifteen to twenty seconds after the injection of sodium cyanide her head felt as if it were enlarging. Respirations gradually increased in depth, reaching their maximum in thirty to forty seconds after the injection. At that time the patient did not respond to questions and at the end of three minutes she still appeared somewhat dazed. Mental work was performed with effort. There was no change in pulse or blood pressure. At the end of fifteen minutes a second injection of 0.04 cc of sodium cyanide was made. The respiratory response occurred in thirty seconds. The patient became restless, her mouth felt dry, and she was confused. When the right carotid sinus was novocainized the injection of 0.03 cc of sodium cyanide produced no symptoms. The effect of a larger amount was not determined.

After operation the patient showed no response to intravenous injections of 0.05, 0.10, 0.15 and 0.20 cc of sodium cyanide. The injection of 0.20 cc caused deepening of respirations at 23 seconds, flushing of the face and drowsiness; her emotional reactions were normal and she was not confused.

Effect of Overventilation

While in the recumbent position, the patient was instructed to breathe deeply and rapidly. This overventilation was continued for a period of six minutes, during which time she was visibly distressed and had to be encouraged to continue. She became confused but not unconscious; her face was cyanotic and the facial veins were prominent; there was tremor of the right hand and arm, quivering of the face, and retching. She sat up, sobbed, trembled, and when able to speak said, "My head feels as if it is flying out into space—it's a horrible feeling. My feet feel cold." Later her feet felt hot. The procedure was repeated a number of times with similar results. The patient remarked that the phenomena provoked by hyperventilation duplicated those portions of her spontaneous attacks that she was able to remember.

After novocainization of the carotid sinus the procedure was repeated. On several occasions overventilation was performed for one to fifteen minutes but none of the above symptoms occurred. There was numbness, tingling, and stiffness of the face, fingers and toes. Chvostek's sign and carpopedal spasms were present. These signs and symptoms were interpreted as indicative of respiratory tetany.

Following denervation, overventilation produced no attacks, and if continued long enough produced signs and symptoms of respiratory tetany.

Effect of Motionless Standing

After resting in the horizontal position for thirty minutes the patient was tilted upright to an angle of 75°. The weight of the body was supported by the feet. The heart rate increased from 70 to 115 beats per minute. The blood pressure fell from 110 systolic, 80 diastolic to 95 systolic, 70 diastolic. At the end of ten minutes she became weak and faint, and on one occasion lost consciousness.

After denervation the patient could stand motionless without developing palpitation and light-headedness. The resting blood pressure was 110 systolic, 84 diastolic, and the heart rate 68. The tilting experiment was repeated. After the patient had stood motionless for fifteen minutes at an angle of 75° the blood pressure was 100 systolic, 70 diastolic, and the heart rate 64. She developed no symptoms of an attack.

*Electroencephalograms before Operation**

At rest. Electroencephalograms with the 8 standard leads showed various gross abnormalities.

*We are indebted to Dr. Frederic Gibbs, of the Neurological Unit, Boston City Hospital for the electroencephalographic studies and for the interpretation of the electroencephalograms. The electrical activity of the brain associated with the carotid-sinus reflex is under investigation in his laboratory and later will be the subject of a more extensive report.

There were many low-voltage, fast (15-to-40-per-second) waves, few or no slow (10-per-second) waves, and occasional runs of square (4-to-6-second) waves. Such abnormalities are seen most frequently during epileptic seizures of the psychomotor and grand-mal types. The records of this patient were therefore interpreted as showing a combination of psychomotor and grand-mal disorders. Analysis of the records by the Grass frequency analyzer⁴ showed a very definite peculiarity. There was much more energy in the fast frequencies than is the case in normal subjects, and instead of showing the narrow peaks at 5, 9½, 28½, 33½ and 43 per second, which are seen in normal subjects, this patient showed wide peaks at 6 per second and multiples of 6 up to 60.

During attacks induced by pressure on the right carotid sinus, by injection of sodium cyanide or by hyperventilation. When seizures were produced by pressure on the right carotid sinus, by the injection of sodium cyanide or by hyperventilation, a definite increase in the abnormalities in the resting record was noted. These changes were essentially the same, regardless of the method employed to precipitate an attack.

The changes in the unanalyzed record appeared to be chiefly an increase in fast activity, but they were not definite enough to be interpreted with certainty. The analyzed records, however, showed that the attacks were associated with a distinct increase in the amount of fast activity. The change was most apparent in the 10-to-25-per-second band. From the electroencephalograms it appears that the patient's attacks were characterized by a shift in cortical activity that is comparable to, but not so extensive as, that seen in association with grand-mal seizures.

After novocainization of the right carotid sinus. Immediately after the right carotid sinus had been novocainized, the abnormal appearance of the resting analyzed record was accentuated. The tendency for broad peaks to occur at 6 per second and intervals of 6 appeared to be more marked than it was before novocainization. However, after ten to fifteen minutes the record became more normal than the pre-novocainized resting record. After novocainization the three procedures that had previously provoked seizures no longer produced a clearly demonstrable increase in fast activity. In one instance the injection of cyanide resulted in a slight increase in fast activity, but this was not comparable to the change that it produced before novocainization. These observations correlate well with the fact that none of the procedures produced seizures after novocainization.

Electroencephalograms after Operation

Records were taken from the eight standard leads. The analysis of resting records taken on December 20, 1939, and February 29, 1940, showed that they were much more normal than before operation, although certain minor abnormalities persisted. There was no longer a tendency for the activity to clump in peaks at intervals of 6 per second. The right frontal and right occipital leads showed strong peaks at $11\frac{1}{2}$ per second, which had not been present before operation. Clinical attacks could not be produced by the injection of cyanide or by hyperventilation. During these procedures the pronounced increase in fast activity that had occurred before the operation was not seen.

Preoperatively, hyperventilation had produced in the period before the onset of the seizure a more marked slowing of cortical activity than is usually seen in normal subjects. After operation this slowing with hyperventilation was less marked, and therefore normal.

DISCUSSION

Weiss and Baker¹ report that convulsions and temporary loss of consciousness can occur without significant changes in the blood pressure or heart rate. Because of the accompanying facial pallor and the fact that the vascular reaction of the facial vessels and meninges are qualitatively alike, they suggest that the cerebral manifestations are the result of vasoconstriction in the brain. Further investigation^{2, 5} revealed that there was no demonstrable cerebral anoxemia during these induced attacks. Moreover, the onset of unconsciousness was more rapid in such cases than in other types of syncope known to be associated with decreased cerebral blood flow.² It was concluded, therefore, that the unconscious state was induced either by the direct action of afferent impulses from the carotid sinus on certain centers in the brain, or by the selective constriction of the vessels supplying these centers. The case described here illustrates this cerebral type of carotid sinus syncope. The attacks induced by pressure on the right carotid bulb usually occurred without a fall in blood pressure or a change in heart rate. The electroencephalograms of the patient during either spontaneous or induced attacks differed from those which are characteristic of anoxemia. This is further evidence that the seizures were caused by a neurological mechanism.⁶

The carotid sinus contains receptors that are sensitive to changes in the endosinial pressure, and receptors that are stimulated chemically by carbon

dioxide, by anoxemia⁷ and by such drugs as sodium cyanide.^{3, 7} In our case, attacks were precipitated by chemical as well as physical stimuli. The intravenous injection of an amount of sodium cyanide which would produce no symptoms in a normal subject caused a seizure. A case with a sensitive carotid sinus of the cerebral type in which the injection of sodium cyanide produced symptoms of faintness has been reported.²

Hyperventilation produced seizures in our patient. The abnormal carotid sinus must have been responsible for the seizures from hyperventilation, since such attacks were not produced post-operatively. Experiments on animals have shown that the alkalosis caused by hyperventilation depresses the activity of the chemoreceptors in the carotid sinus.⁷ Therefore it is unlikely that hyperventilation stimulated the abnormal carotid sinus in our patient. Hyperventilation reduces the blood flow in the human brain.⁸ It thus appears that the combination of decreased flow of cerebral blood from hyperventilation and the afferent impulses from the abnormal carotid sinus was sufficient to cause a seizure. When the latter were inhibited by novocainization or denervation, hyperventilation did not cause an attack. Similarly, the syncope with the patient in the upright position may be explained by the effect of an abnormal carotid sinus on a brain in which the blood flow was reduced by gravity.

Because of the family history of fainting attacks, the history of migraine and the abnormal electroencephalograms, it was assumed that this patient had idiopathic epilepsy, and that the right carotid sinus served as a trigger mechanism to produce attacks in a brain that was already abnormal. The fact that the production of seizures by stimulation of the carotid sinus was followed by even more abnormalities than were present in the resting state supported this explanation. Further study showed that the right carotid sinus must have been responsible for most of the abnormally fast activity seen in the analyzed electroencephalograms, since the fast activity decreased after novocainization and denervation. This suggested the possibility that in this case the abnormal carotid sinus was the primary mechanism, and that as a result of prolonged hyperactivity it had produced permanent minor changes in the brain. The data needed to decide this point are not available.

The evidence that afferent impulses from a peripheral receptor organ may exert a continual influence on cerebral activity, and that this influence can be removed by denervation of the peripheral receptor, is of fundamental importance. The extent to which the normal carotid sinuses

influence the normal human brain is unknown. It has been reported that in normal animals there are continuous afferent stimuli which arise from the pressor⁹ and chemoreceptors⁷ in the carotid sinus. Hering¹⁰ believes that these stimuli are essential for maintaining the tone of the autonomic nerve centers.

The cause of idiopathic epilepsy is obscure. It has been reported that the disease is associated with a paroxysmal cerebral dysrhythmia,¹¹ and that in the majority of cases a sensitive carotid sinus has played no part in causing the symptoms. In certain epileptic patients it may act as a trigger mechanism and initiate seizures. In this patient it appears that the sensitive carotid sinus was of primary importance, not only in precipitating attacks but also in modifying the brain waves between attacks. Even though such cases may be extremely rare, they should be searched for carefully, because relief of symptoms may be obtained by a relatively simple surgical procedure.

SUMMARY

Studies of a patient with migraine, atypical epilepsy and a sensitive right carotid sinus of the cerebral type are presented. These atypical epileptic attacks were induced experimentally by external pressure on the sensitive carotid sinus, by intravenous injection of sodium cyanide and by overventilation.

Following novocainization of the sensitive carotid sinus, and its surgical denervation, attacks were not produced by the procedures listed above. There have been no spontaneous attacks since operation.

Electroencephalographic studies in the resting state before operation showed changes compatible with psychomotor and grand-mal epilepsy. After

operation the electroencephalographic record revealed a decrease in this abnormality. Electroencephalographic studies during attacks induced by external pressure, by cyanide or by overventilation caused an increase in the abnormal activity noted at rest.

The evidence indicates that in this case a sensitive carotid-sinus mechanism of the cerebral type played a significant role in the clinical seizures and in the production of the abnormalities observed in the electroencephalograms. The changes in the latter were not those of anoxemia.

These studies furnish further evidence that a peripheral autonomic receptor organ, that is, the carotid sinus, can produce seizures by the direct effect of afferent impulses on the brain.

REFERENCES

1. Weiss, S., and Baker, J. P. The carotid sinus reflex in health and disease its role in causation of fainting and convulsions. *Medicine* 12:297-354, 1933
2. Ferris, E. B., Jr., Capps, R. B., and Weiss, S.: Carotid sinus syncope and its bearing on the mechanism of unconscious state and convulsions study of thirty-two additional cases. *Medicine* 14:377-456 1935
3. Heymans, C., Bouckaert, J. J., and Dautrebande, L.: Sinus carotidiens et réflexes respiratoires III. Sensibilité des sinus carotidiens aux substances chimiques. Action stimulante respiratoire réflexe du sulfate de sodium, du cyanure de potassium, de la nicotine et de la lobeline. *Arch internat de pharmacodyn. et de therap.* 40:54 91, 1931
4. Grass, A. M., and Gibbs, F. A.: A Fourier Transform of the electroencephalogram. *J Neurophysiol.* 1:521-526, 1938
5. Lennox, W. G., Gibbs, F. A., and Gibbs, E. L.: Relationship of unconsciousness to cerebral blood flow and to anoxemia. *Arch. Neurol. & Psychiat* 34:1001 1013, 1935
6. Gibbs, F. A., Williams, D., and Gibbs, E. L. Modification of the cortical frequency spectrum by changes in CO₂, blood sugar and O₂. *J. Neurophysiol* 3:49 58, 1940
7. Samman, A., and Stell, G.: The response of the chemical receptors of the carotid sinus to the tension of CO₂ in the arterial blood in the cat. *J Physiol* 85:309 319, 1935
8. Gibbs, F. A., Gibbs, E. L., and Lennox, W. G. Changes in human cerebral blood flow consequent on alterations in blood gases. *Am J Physiol* 111:557 563, 1935
9. Bronk, D. W., and Stell, G. Afferent impulses in the carotid sinus nerve 1 The relation of the discharge from single end organs to arterial blood pressure. *J Cell. & Comp Physiol* 1:113-130, 1932
10. Hering, H. E. *Der Blutdruckreglerionus in seiner Bedeutung für der Parasympathikus-tonus und Sympathikus-tonus.* 48 pp Leipzig Georg Thieme, 1932
11. Gibbs, F. A., Gibbs, E. L., and Lennox, W. G. Epilepsy a paroxysmal cerebral dysrhythmia. *Brain* 60:377 388, 1937.

NONTRAUMATIC DISLOCATION OF THE ATLANTOAXIAL JOINT*

SAMUEL S. HANFLIG, M.D.,† AND CHARLES SCHLOSBERG, M.D.‡

CAMBRIDGE, MASSACHUSETTS

A CASE of unilateral dislocation of the atlas on the axis, unassociated with or related to injury, is presented. This is a rare type of dislocation, and the case reported herein is interesting because it demonstrates the ease with which the diagnosis may be overlooked for a long period. It also reaffirms the importance of proper x-ray studies, particularly an anteroposterior view through the mouth, in establishing the diagnosis. The case is of further interest because it establishes the fact that a rather long period during which the diagnosis may be overlooked does not necessarily prevent a satisfactory and lasting reduction of the dislocation.

Nontraumatic dislocation of the atlas on the axis has been recognized and described for many years. Corner¹ in 1907, in describing rotatory dislocation, suggested that it could be produced by trauma so slight as to be negligible. The mechanism of the production of such a dislocation is best understood by a brief consideration of the anatomy of the atlantoaxial joint.

ANATOMY

The lateral joint surfaces between the atlas and axis are oval-shaped and essentially plane, with their surfaces directed slightly downward, forward and outward. Each joint has a loose capsular ligament and a synovial sac. The ligaments are strengthened in front and behind by the anterior and posterior atlantoaxoid ligaments. The transverse ligament is a strong, tightly woven fibrous band that passes across the large central opening in the arch of the atlas and divides it into a small anterior portion, through which the odontoid process projects, and a large posterior part, which is the upper continuation of the spinal canal, and which transmits the spinal cord, its membranes and the spinal portion of the associated spinal nerves.

Motion between the atlas and axis is mainly rotation, whereas that between the head and the atlas is flexion in the sagittal direction with slight lateral motion. Anterior dislocation of the atlas on the axis can occur with rupture or relaxation of the transverse ligament. Obviously, there can be no rupture of the transverse ligament unless there is severe trauma. Consequently in the non-

traumatic variety one is probably dealing with a relaxation of the transverse ligament. The vast majority of nontraumatic dislocations are forward and anterior with some degree of rotation. Berkeheiser and Seidler² have suggested that the anterior type predominates because the center of gravity of the head is farther forward than the anatomic support.

ETIOLOGY

Fairly constant in these clinical pictures is a pre-existing infection of a type that can produce a hyperemia at the base of the skull, such as tonsillitis, pharyngitis, adenitis and mastoiditis. As to the mechanism by which the focus effects such a relaxation, there is a difference of opinion. Wittek³ believed that the effusion might develop between the odontoid process and the anterior arch of the atlas, and between the odontoid process and the transverse ligament of the atlas, with resulting softening and stretching and relaxation of the transverse ligament. Jacobs¹ suggested that the atlaoxoid articulation might become distended and result in spontaneous dislocations. He compared it with the pathologic dislocations of the hip joint seen in typhoid fever and, agreeing with Wittek,³ termed it a distention luxation of the joint. Greig⁷ in 1931 published the results of his investigations on the effect of hyperemia on bones, and established the fact that hyperemia may produce decalcification.

Watson-Jones⁶ and Jones⁷ believe that the hyperemia produces a decalcification of the anterior and lateral part of the ring of the atlas, with softening and loosening of the attachment of the transverse ligament. Such a theory is favored by the fact that this condition occurs so frequently following an acute infection of a type that can produce hyperemia in the region of the base of the skull, and is further favored by the fact that such atlantoaxial dislocations occur mostly in young children whose bones are very vascular. As a result of relaxation of the transverse ligament or capsular ligaments of the articulations, with a normal movement the articular facet of the atlas may slip over the anterior marginal lip of the facet of the axis, producing a forward dislocation.

CLINICAL FEATURES

The usual history is that following an acute tonsillitis, pharyngitis, adenitis or similar infection,

*From the Orthopedic Service, Cambridge Hospital.

†Junior orthopedic surgeon, Orthopedic Service, Cambridge Hospital.

‡Formerly, Intern, Cambridge Hospital.

a painful, stiff neck developed. The head is held rigid, slightly ahead of its normal plane; the occiput is rotated toward the shoulder on the side of the dislocation, and the chin is held close to the neck and rotated to the other side. It is the ordinary position of a wry neck, without, however, any spasm of the sternocleidomastoid muscles. There is impairment of rotatory motion of the head on the neck. The mouth cannot be opened actively or passively beyond a very limited extent. A reduction in the size of the posterior nasopharynx, due to the projecting anterior arch of the atlas, is present and can be determined by palpation through the mouth. The transverse process of the atlas is not palpated in its usual position on the side where the transverse process is displaced backward. The head is tilted toward the side on which the atlas has been dislocated forward. The spine of the second cervical vertebra can be palpated on the opposite side. Rarely, there may be neurologic signs. The patient tends to support the chin in his cupped hand.

Watson-Jones⁶ in his first case demonstrated that half the anterior arch of the atlas had disappeared. He stated that if it were not for later x-ray photographs, one might suspect a congenital anomaly or bony destruction due to disease. Subsequent x-ray films showed the arch again united, so that Watson-Jones concluded that the defect was caused by decalcification. Accordingly, this defect in the arch due to decalcification must be sought for in the x-ray film. In addition, one must look for the other x-ray signs, which may be difficult to demonstrate; because of the position of the lesion and the sensitiveness of the neck painstaking efforts are usually necessary to secure adequate pictures. A correct lateral view will show the atlas held forward in an altered position. An anteroposterior view taken through the mouth will show a narrowing or obliteration of the joint through the facets and an eccentric odontoid process. This view similarly is hard to obtain because the patient may have difficulty in opening the mouth sufficiently.

TREATMENT

Early cases that are not very severe usually respond to traction with a Sayre sling in the recumbent position on a slightly hyperextended frame. The reduction may be prompt or prolonged. Following reduction, which must be checked not only by the physical but by x-ray examination, a plaster-of-Paris cuirass with the head extended is applied. More resistant cases may necessitate the use of anesthesia and manipulation for the purpose of

reduction. The method first described by Walton¹ is still perfectly satisfactory. Briefly, the maneuver consists of freeing the dislocated articular facet of the upper vertebra by lifting it free in the flexed position, and then rotating it into place by dorso-lateral flexion, followed by rotation. The patients, in whom reduction is impossible because the dislocation has been unrecognized for a long period may accommodate themselves to the changes without any particular harm, although they are prone to sudden severe accidents and the development of a myelitis at some later date. Operative intervention has been described for old unreduced cases of atlaxial dislocation. Mixer and Osgood⁷ describe such an operative procedure.

Following successful reduction checked by satisfactory x-ray films, immobilization in plaster of Paris for a period of four to six months is advised. This should be followed by the use of a Thomas collar for an additional two to four months. Following this, physiotherapy and graded exercises are instituted.

CASE REPORT

L. P., a 7-year-old schoolboy, was admitted to the Cambridge Hospital on January 15, 1936, because of an upper-respiratory infection, cervical adenitis and functional torticollis of 1 month's duration. He had been apparently well up to January 1, 1936, at which time he had a severe "head cold," followed by cervical adenitis. He had had tonsillitis repeatedly during the last several years. For the 3 weeks prior to admission he had received heat locally, without much improvement. The past history was essentially non-contributory.

Physical examination showed a well-developed and fairly well-nourished boy whose head was tilted to the left and flexed in the forward position. The trapezius muscle on the right side was hard and taut. There was a chain of enlarged lymph nodes in the right posteroauricular and cervical regions. The tonsils were cryptic and somewhat enlarged. The rest of the examination was negative. A preliminary diagnosis was made of cervical adenitis, possible tuberculosis and functional torticollis.

X-ray films taken in the usual manner were interpreted as negative. No view through the mouth was taken, and the lateral view was unsatisfactory because of the difficulty in securing it with the head in its position of torticollis. The patient was seen in consultation by a member of the Nose and Throat Service, who recommended tonsillectomy and adenoidectomy. This operation was performed on February 7, and the patient was discharged relieved on February 12. The day after discharge the head was in the same position that it had been on admission, that is, tilted to the left with the chin held down and toward the right. The patient was shortly thereafter taken to the outpatient department of another hospital, and was there referred from the pediatric clinic to the orthopedic clinic. X-ray photographs revealed "possible fracture of the first cervical vertebra, with displacement laterally to the left, and possible fracture, compression type, of the third cervical vertebra." It was noted that there had been no history of trauma. On March 6 the patient was admitted to that hospital. Physical examination revealed

a child who was poorly nourished, and whose head was bent to the left. He was unable to move his head because of rigidity. He could not make a sudden move in any direction, and the neck was splinted by muscle spasm. The patient was put in head traction (5 pounds). On March 22 he was able to move his head within a wide range, and on March 27 could move his head in all directions. On March 30 the head traction was removed and the patient was still able to rotate his head in all directions. On April 4 some of the limitation returned shortly after the patient was allowed to get up. The head and neck were placed in a plaster cast of the cuirass variety, and the patient was discharged home.

The cast was kept on until May 12, at which time infra-red therapy, massage and exercises were instituted. An attempt was made to carry out traction at home, but this proved unsatisfactory.

On June 3 the patient returned to the Orthopedic Department of the Out-Patient Department of the Cambridge Hospital. Physical examination showed the same type of torticollis that was present at the original admis-

sion. A click was felt during the procedure, and post-reduction x-ray examination showed complete reduction of the dislocation. A plaster cast was applied to the head and cervical spine, in slight hyperextension, the cast extending down over the trunk to enclose the pelvis. X-ray examination on October 9



FIGURE 2. Anteroposterior View through the Mouth.

This shows obliteration of the articular joint space on the left side, due to slipping forward of the articular facet of the atlas on the axis. Note the eccentric position of the odontoid process.



FIGURE 1. Lateral View.

There is anterior displacement of the atlas on the axis.

sion. X-ray photographs were again taken, but failed to disclose the cause of the deformity. The patient was discharged and referred to the Physiotherapy Department. On July 22, examination in the Out-Patient Department still showed torticollis, but it was less marked. A group of lymph nodes were discovered at the lower right occiput, and it was thought that this condition might be a factor in the persistence of the torticollis. Compresses were advised, and finally on September 9, after much technical difficulty in securing x-ray films of the cervical spine, lateral and anteroposterior views through the mouth showed an anterior displacement of the atlas on the axis, with forward displacement of the articular facet on the left (Figs. 1 and 2). No evidence of fracture could be discovered.

The patient was readmitted to the Cambridge Hospital on September 20 and was put in head traction (4 pounds). This produced no change in the condition of the neck, and x-ray films revealed no change from those taken on September 9. On October 5, with the patient under general anesthesia, the dislocation was reduced. The method employed was further flexion of the head onto the chest, and lifting up, extending and rotating the head to the

right and the chin to the left. The patient was discharged home on October 11, and was followed in the Out-Patient Department. The cast was kept on until



FIGURE 3. Lateral View.

The dislocation of the atlas on the axis has been reduced.

January 29, 1937, at which time it was removed and a Thomas collar was applied.

X-ray examination on February 17 showed that the position and alignment of the cervical spine were still good (Figs. 3 and 4). There was still a good deal of stiffness of the cervical spine, for which physiotherapy and graded exercises were begun. On June 2 the patient was completely well, except for a tendency to carry the head

slightly forward. The Thomas collar was discarded late in June. The patient spent the summer at Children's Island, a convalescent home for children, but had to be sent home because of behavior problems. The superintendent wrote that he turned somersaults by putting his head on the ground, then throwing himself over. The pa-



FIGURE 4. Anteroposterior View through the Mouth.

This demonstrates the restoration of the interarticular joint space on the left. The odontoid process has been replaced in its usual mid-line position.

tient was seen frequently, and on November 3 he had complete and normal motion, but there was still a tendency to tilt the head slightly. He was last seen on November 8, 1939, at which time his family stated that he had had no recurrence of pain, stiffness or deformity of the neck. Physical examination was completely negative. The head was held erect in the proper position, and all motions were complete and painless.

CONCLUSION

A case of spontaneous dislocation of the atlanto-axial joint is presented.

It emphasizes the fact that an atlantoaxial dislocation must be thought of in the examination of any torticollis that occurs in a patient who also has infection in the cervical region or its vicinity. It also demonstrates that it is difficult to obtain satisfactory x-ray photographs of the cervical spine when there is a torticollis, and that such exposures must be judged unsatisfactory for the detection of this disorder, unless in the lateral view the first and second cervical vertebrae are outlined satisfactorily, and unless one can secure a satisfactory view of the same area through the mouth.

It is important to note that long delay in making a diagnosis does not render impossible a satisfactory reduction. In this case the dislocation had existed for almost ten months before it was satisfactorily reduced by manipulation under anesthesia. The reduction has persisted for an interval of three and a half years.

REFERENCES

1. Corner, E. M.: Rotary dislocations of the atlas. *Ann. Surg.* 45:926, 1907.
2. Berkeheiser, F. J., and Seidler, F.: Nontraumatic dislocations of the atlanto-axial joint. *J. A. M. A.* 96:517-523, 1931.
3. Wittek, A.: Ein Fall von Distensionsluxation in Atlanto-epistrophe Gelenke. *Munchen. med. Wchnschr.* 55:1836, 1908.
4. Jacobs, C. M.: Atlas and axis luxation. *Am. J. Ortho. Surg.* 16:357-364, 1918.
5. Greig, D. M.: *Clinical Observations on the Surgical Pathology of Bone*. 248 pp. Edinburgh and London Oliver and Boyd, 1931.
6. Watson-Jones, R.: Spontaneous hyperaemic dislocation of the atlas. *Proc. Roy. Soc. Med.* 25:586-590, 1932.
7. Jones, A. R.: Dislocation of the neck of the atlanto-axial joint. *Proc. Roy. Soc. Med.* 26:136, 1932.
8. Walton, G. L.: Dislocation of the cervical vertebrae: five cases recovered without operation. *Boston M. & S. J.* 120:277-281, 1889.
9. Mixter, S. J., and Osgood, R. B.: Traumatic lesions of the atlas and axis. *Ann. Surg.* 51:193-207, 1910.

REPORT ON MEDICAL PROGRESS

SOME EPIDEMIOLOGICAL CONSIDERATIONS OF DIPHTHERIA

VLADO A. GETTING, M.D.*

BOSTON

THE presence or absence of diphtheria in any community depends on three factors—the host, the *Corynebacterium diphtheriae* and the environment. The epidemiology of diphtheria is the study of the interrelation of these three, of the variations of one and the resulting effects on the others. The control of diphtheria is largely dependent on the understanding of these phenomena and the institution of measures to bring about conditions more favorable for the limitation of the disease.

NATURAL IMMUNITY

Diphtheria is a struggle of survival between the infecting organism, *C. diphtheriae* and the infected host, man. If both are to survive, the host and the parasite must reach an equilibrium, otherwise, either man overcomes the *C. diphtheriae* and thereby destroys it, or the parasite kills man and in turn deprives itself of a means of survival. The history of diphtheria is an account of this struggle of survival, which is not a static but an active and progressive phenomenon. The ideal state for both man and *C. diphtheriae* is reached when a state of symbiosis develops in which the parasite can continue to live in the throat without serious injury to the host. This symbiotic or carrier stage results only after prolonged adjustments between the host and the parasite and involves changes in one or the other or both.

The changes in the host are not only in the individual but in the entire population or community. Generally, resistance of the host depends on two factors, natural and acquired immunity. The host inherits through his genetic constitution a certain capacity of resistance or ability to develop immunity. In addition to the universal race immunity, there is individual variation, depending on the immunizability inherited from the host's parents. Through environmental contact this immunizability can be developed into acquired immunity. Immunity to diphtheria can be acquired by contact with *C. diphtheriae*. The titer of the diphtheria antibodies depends in part on the constitutional capacity to produce and maintain the titer. Contact between the host and diphtheria

bacilli may result in a carrier state or in a subclinical or unrecognized infection of the host. The immunity in a population acquired by these experiences is termed latent. Usually, this latent resistance of a community is characteristic and varies from one community to another, depending on its experience with *C. diphtheriae*. In the newborn, temporary passive immunity may be acquired from the mother, since the mother's diphtheria antitoxin passes through the placenta into the fetal circulation. Such passive immunity commonly disappears at the age of six to nine months.

The immunity of a population is a variable factor, it changes from place to place and from generation to generation. The degree of natural immunity present in any community at any given time is dependent on its experience with *C. diphtheriae*, on the number of avirulent and virulent carriers, on the type of organism prevalent, on the number of cases of diphtheria and on the density and age of the population. Recent evidence¹ suggests that natural community resistance is highest where there is a high virulent carrier rate, where the gravis type of *C. diphtheriae* is prevalent, where cases of diphtheria are more frequent, where the population is dense or in places where these conditions have been recently current. Avirulent carriers, however, may also be responsible for producing community resistance. The lowest natural immunity is found in rural areas where there is neither the disease nor carriers. Diphtheria is most likely to occur in a locality where the immunity is low, where there are frequent contacts among a young population and where the diphtheria organism becomes prevalent. The presence of diphtheria in a community increases its immunity, but usually at the cost of increased morbidity and mortality. The immunity of a locality may be increased by systematic immunization of pre-school and school children.

Schick testing is a routine procedure, is no longer considered essential either before or after immunization, except in a patient in whom the physician may wish to ascertain the presence or absence of sufficient immunity. Schick testing surveys, however, are of value in estimating the level

*Assistant in epidemiology, Harvard Medical School and Harvard School of Public Health; epidemiologist, Division of Communicable Diseases, Massachusetts Department of Public Health.

of the locality's immunity, as was done by Gill² in Alabama, where 89 per cent of 2510 white children six to fifteen years old were without a history of previous immunization and were Schick negative. In Virginia³ of 2445 children tested 70 per cent gave negative reactions—77 per cent of those previously immunized and 60 per cent of those uninoculated. Observations in Cleveland⁴ reveal that the annual increment of negative Schick reactions in children aged five to fourteen years, who had not been immunized, averaged 2.5 per cent yearly with the result that only 36 per cent of the children of age fifteen were Schick negative. It is apparent that the results of these surveys cannot be applied to other localities, and that the immunity as determined by the Schick test varies in different communities.

ARTIFICIAL IMMUNIZATION

Present methods of controlling diphtheria as a community disease depend largely on active arti-

produced both primary and secondary stimulus effects and thereby resulted in a sufficiently high immunity. Recently, the Subcommittee on Diphtheria of the Committee on Evaluation of Administrative Practices of the American Public Health Association⁵ completed a critical study of the efficiency of community immunization, using various doses of fluid toxoid and alum-precipitated toxoid. These studies were made over a period of four years on 2523 children. The level of immunity reached after immunization was determined by titration of the antibodies present in the blood at intervals ranging up to thirty-six months after immunization. These workers have demonstrated that two doses of alum-precipitated toxoid, administered three weeks apart, gave the highest percentage of children with a demonstrable level of antitoxin in the blood. The results with three doses of fluid toxoid were very nearly as satisfactory, and those with one dose of alum-precipitated toxoid were sufficiently good to warrant its use

TABLE 1. *Comparison of Antitoxin Response to Different Immunizing Procedures.**

PROCEDURE	INTERVAL BETWEEN FIRST INJECTION AND ANTITOXIN TITRATION											
	4 MONTHS			12 MONTHS			24 MONTHS			36 MONTHS		
	No. of cases	.001 unit or more	.01 unit or more	No. of cases	.001 unit or more	.01 unit or more	No. of cases	.001 unit or more	.01 unit or more	No. of cases	.001 unit or more	.01 unit or more
Two injections fluid toxoid (3-week interval)	240	65.5	32.5	183	57.9	27.9	114	50.8	24.6	—	—	—
One injection alum-precipitated toxoid	413	92.0	58.1	379	88.1	49.0	361	79.8	36.6	120	70.0	23.3
Three injections fluid toxoid (3-week intervals)	393	96.2	71.2	203	94.2	64.5	51	92.2	68.6	—	—	—
Two injections alum-precipitated toxoid (2-week interval)	332	100.0	96.0	203	100.0	92.7	—	—	—	—	—	—

*Taken from Volk and Bunney.⁵ All children had less than 0.001 unit of antitoxin per cubic centimeter of serum at the time of the first injection.

ficial immunization. In 1913, Von Behring reported successful immunization of children with toxin-antitoxin mixtures, and rapid development of immunization technic has continued to the present. After a primary stimulus, produced artificially by injection or naturally by infection, the titer of antibodies is low; after the second stimulus there is, however, a greater and more rapid response, and the antibody titer reaches a much higher level. Subsequent stimuli tend to raise the titer. Because natural immunity is frequently absent in young children, it is desirable to provide both primary and secondary stimuli in artificial immunization. Most methods therefore require the administration of more than one dose of antigen. Alum-precipitated toxoid was introduced by Glenny on the hypothesis that because of the delayed absorption of the toxoid a single injection

under certain circumstances. Two doses of fluid toxoid did not give a high percentage of immunity. The comparison of antitoxin response to the different immunizing procedures is summarized in Table 1.

As a result of these studies, the Committee on Evaluation of Administrative Practices⁶ has recommended that two doses of alum-precipitated diphtheria toxoid with a four-week or one-month interval between doses, or three doses of fluid toxoid at four-week or one-month intervals are the preferred practice for pre-school and school children under ten years of age. In 1932, Godfrey⁷ stated that the immunization of 30 per cent or more of the group under five years of age, in addition to more than 50 per cent of children five to nine, is adequate to produce a striking decline in the diphtheria rate of a community. The "Ap-

praisal Form for Local Health Work" of the American Public Health Association⁸ evaluates the immunization of pre-school children as five times as high as the immunization of elementary school children. A community immunization program should be aimed at the under-five age group, which contains the highest proportion of susceptible children. Prevention of diphtheria in infants reduces not only morbidity but also mortality, because case-fatality is highest under two years of age and decreases with increasing age.

TYPES OF *C. DIPHTHERIAE*

Diphtheria has been steadily decreasing in the United States since the latter part of the nine-

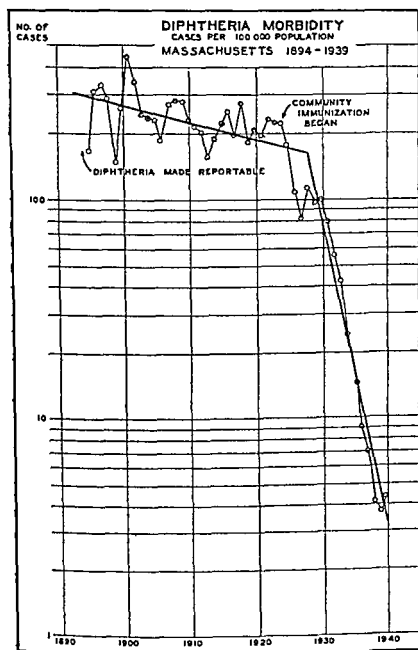


FIGURE 1. Diphtheria Morbidity.

The heavy line represents the calculated trend. There is a gradual decrease in morbidity until 1927, and a more rapid decrease thereafter.

teenth century. Figure 1 shows the decline that occurred in Massachusetts. Up to about 1925, the decline was gradual and apparently due to natural causes. About 1923, artificial immunization became a widespread community practice, and thereafter the decline of diphtheria was accelerated.

Undoubtedly, natural causes still play a role in the more rapid decline. One of these natural causes has been discussed as latent immunity. Changes in *C. diphtheriae* are another important natural cause. Diphtheria is one of the diseases that fluctuate in prevalence and involve periods of many years. During the last sixty years we have been on the downward slope of such fluctuation. This fluctuation may be due, in part, to intrinsic changes in *C. diphtheriae* that affect the virulence, invasiveness and toxigenicity of the organism.

Whether the various types described by Anderson et al.⁹ arose during recent years is a matter of speculation. But as a result of observing the fluctuations of infectiousness and toxigenicity in diphtheria organisms at Leeds during an outbreak of unusually severe diphtheria, the authors determined that the organisms from the malignant or fulminating cases were culturally different from strains isolated from milder cases; they divided the strains of *C. diphtheriae* into three types—*gravis*, *intermedius* and *mitis*. The *gravis* type, associated with severe toxic cases, is characterized culturally by a granular deposit and pellicle formation in broth, by flattened lusterless colonies of irregular outline on chocolate tellurite media and by fermentation of polysaccharides. The *mitis* type was isolated from milder cases in which there was extensive membrane formation, without toxic manifestation but with obstructive symptoms. The cultural characteristics of *mitis* organisms are uniform turbidity in broth, convex, partly translucent and light-reflecting colonies on chocolate tellurite media and no fermentation of polysaccharides. About 5 to 10 per cent of the strains were of the *intermedius* types, which are characterized by granular growth in broth but no fermentation of polysaccharides.

Some authors have been unable to correlate these cultural characteristics with the clinical severity of cases. The *gravis* organism is a poor toxin producer as determined in the laboratory. Judged by present methods, the *gravis* organism may be avirulent, or cause mild cases. It is entirely possible, however, that the clinical association of toxicity observed in *gravis*-type infections is not adequately tested by present laboratory procedures. Field data indicate that the prevalence of the *gravis* type may be associated with increased morbidity and mortality. Data collected by Frobisher¹ suggest that in Virginia and Alabama the virulent *gravis* organism has been increasing in prevalence during the past two years, whereas in certain northern communities the *mitis* type is more prevalent. This observation becomes significant when it is remembered that in the past decade mortality has de-

clined much more rapidly in the North than in the South.

There is a marked difference in the prevalence of types of *C. diphtheriae* in various localities, and even from year to year in the same locality. Aside from purely bacteriological differences, this variation of the prevailing type of organism may have fundamental importance. It is not unlikely that the determination of fluctuations in the prevailing types may be correlated with morbidity and mortality rates and with latent immunity, and that it may thereby furnish a base line for the evaluation and administration of the methods of diphtheria control. The prevalence of mitis type is associated with low immunity and low morbidity. The shift of the prevailing type from mitis to intermedius and gravis types may indicate increased morbidity and mortality, and may forecast to public-health officials the trend of the disease to be expected in the community.

DIPHTHERIA CARRIERS

Diphtheria is a respiratory disease usually spread by carriers of virulent organisms. Carriers may be either convalescent and temporary or chronic, as a result of sub-clinical infection or previous disease. Hartley and Martin¹⁰ determined the rate at which the diphtheria organism disappeared from the throats of convalescents. The rate of disappearance depends on the type of organism, the treatment, reinfection and the criterion of the tests applied. These workers used as their standard three successively negative cultures taken at weekly intervals, and calculated the date of disappearance of the organisms as midway between the last positive and the first of three negatives. They determined that after the fifth day of admission there was a constant logarithmic decrease in the number of carriers, and that an individual who had carried organisms in his throat for six weeks was just as likely to become free during the next week as one who had carried the organisms for only one week. About 5 per cent of those who were carriers one day gave negative cultures the following day. This decrease continued during the fifty days in which the patients were under observation, and 10 per cent of the original group remained carriers at the end of this period.

Most diphtheria carriers, however, have sub-clinical infections and have never had the disease. Carrier rates vary in different localities, from year to year, and from season to season. It is to be noted in Frobisher's figures¹ that natural immunity appears to run roughly parallel to the carrier rate. Virulent carrier rates are higher in the South than in the North. In Alabama, with

a carrier rate of 5.4 per cent, there was a high natural immunity (80 per cent at ages five to fourteen), although less than 40 per cent of the organisms in carriers were virulent. In Kingston, New York,¹¹ where 1700 children were cultured, there were no virulent carriers, and 1.55 per cent avirulent carriers associated with 30 per cent naturally immune in the five-to-fourteen age group. This observation indicates that avirulent carriers may play an important role in the latent immunization of a community.

Although other lymphoid tissue and the mucous membrane of the nose and throat may be involved, the localized infection responsible for the chronic carrier state is usually limited to the faucial tonsils. The organisms may be limited to the surface epithelium, but more commonly invade the crypts and are discharged in a fibrinous exudate. Some carriers discharge organisms solely from the nose, and in these the lesion is associated with injury of the nasal mucosa or that of the accessory sinuses. Diagnosis of a carrier can be made only by culturing the organisms from swabs that have been stroked over the tonsils and the posterior nasal mucosa. Carriers should be considered sources of dangerous infection until proved otherwise, and should be isolated to prevent the spread of diphtheria. In Massachusetts¹² all convalescent patients and contacts of cases are required to have two negative nose and throat cultures taken at an interval of twenty-four hours before they are released, unless it is demonstrated that the organism is avirulent.

Treatment of the carrier to remove the infection has usually proved unsatisfactory. Diphtheria antitoxin has no effect on the carrier stage. Local applications of various disinfectants and drugs have been of no avail. Tonsillectomy has proved effective in removing the infection from faucial carriers. This operation should not be performed until at least six weeks have elapsed since the acute attack, because toxic myocarditis¹³ may be present.

NEW DIAGNOSTIC PROCEDURES

In every case of acute upper-respiratory infection with definite membrane formation, diphtheria should be considered and the infection treated as such until proved otherwise. The diagnosis is confirmed by finding diphtheria organisms in cultures taken from the suspicious membrane in the nose or throat. Various culture mediums have been tried in an attempt to accelerate the growth of *C. diphtheriae* and inhibit that of other organisms. Several modifications of Clauberg's medium have been investigated as a substitute for the slower Löffler's medium. Most investigators^{14, 15} agree

that *Clauberg's medium* is not a substitute but rather an adjuvant to *Löffler's medium*, and that it is apt to give many false positives. Many laboratories have utilized small test tubes containing but 1 cc. of *Löffler's medium* and have found these to be quite effective and more economical, provided they are kept moist. The tubes containing the broken-off swab and sealed with a rubber stopper¹⁶ may be kept in the vest pocket for three to four hours at body temperature and still give satisfactory results. Experienced laboratory technicians are able to identify diphtheria bacilli in direct smears made from swabs that are moist and have been stroked vigorously over the membrane.

The Manzuillo test^{17, 18} for the diagnosis of diphtheria consists of rubbing a swab, which has been treated with 2 per cent potassium tellurite, over the suspected membrane; whereupon diphtheria organisms become distinguished from others by assuming a black discoloration. This test, however, is not reliable, because it has produced a very high percentage of false positives and some false negatives. The most reliable diagnostic procedures remain direct smear and culture on Löffler's medium. For the typing of *C. diphtheriae* according to colony characteristics, chocolate or blood tellurite agar has proved most satisfactory.¹⁹

REFERENCES

- 1 Frohner, M. Jr. Strains of *C. diphtheriae* in various parts of the United States. *Am J Pub Health*, Supp 30 28 35, 1940
- 2 Gill, D. G. Schick test and carrier surveys in white school children in Alabama, 1937-1938. *Am J Pub Health*, Supp 30 27, 1940
- 3 Grossman, W. A. Schick test and diphtheria carrier survey of white school children in Virginia. *Am J Pub Health*, Supp 30 8 15, 1940
- 4 Schmitt, L. M., and Doull, J. A. Diphtheria infection and morbidity in Cleveland, 1937-1939. *Am J Pub Health*, Supp 30 16-24, 1940
- 5 Volk, V. K., and Bunney, W. E. Diphtheria immunization with fluid toxoid and alum precipitated toxoid progress report. *Am J Pub Health*, Supp 30 42, 1940
- 6 Committee on Evaluation of Administrative Practices, American Public Health Association. Recommended diphtheria immunization procedures. *Am J Pub Health*, Supp 30 1, 1940
- 7 Godfrey, E. S., Jr. Practical uses of diphtheria immunization records. *Am J Pub Health* 23 809 812, 1933
- 8 *Appraisal Form for Local Health Work, 1938* 185 pp. New York: American Public Health Association, 1938
- 9 Anderson, J. S., Hapgood, F. C. McLeod, J. W., and Thomson, J. G. On the existence of two forms of diphtheria bacillus—*B. diphtheriae grauei* and *B. diphtheriae mitis*—and a new medium for their differentiation and for the bacteriological diagnosis of diphtheria. *J Path. & Bact.* 34 667 681, 1931
- 10 Hartley, P., and Martin, C. J. The apparent rate of disappearance of diphtheria bacilli from the throat after an attack of the disease. *Proc Roy Soc Med* 13 277 289, 1920
- 11 Stebbins, E. L. Diphtheria immunity and carrier surveys in New York State. *Am J Pub Health*, Supp 30 36 41, 1940
- 12 of Public Health. *New*
- 13 of cardiovascular disease in diph
- 14 Murray, J. F. A comparison of Clauberg's and Löffler's media in the laboratory diagnosis of *C. diphtheriae*. *South African M J* 13 506, 1939
- 15 Grossman, H., and Grasnuck, L. Vergleichende Untersuchungen über den Diphtheriebacillennachweis mit den Nahboden II und III nach Clauberg. *Med Klin* 35 1317 1319, 1939
- 16 Barksdale, I. S. A new and more practical culture tube designed for in the diagnosis of diphtheria. *Pp* 790 792
mediate tellurite test in diphtheria
ebacterium diphtheriae in Baltimore

MASSACHUSETTS MEDICAL SOCIETY

PROCEEDINGS OF THE COUNCIL

Stated Meeting, October 2, 1940

A STATED meeting of the Council of the Massachusetts Medical Society was held in John Ware Hall, Boston Medical Library, 8 Fenway, Boston, on Wednesday, October 2, at 10:30 a.m. The president, Dr. Walter G. Phippen, Essex South, was in the chair, and 234 councilors (Appendix No. 1) were present.

After calling the meeting to order, the President spoke as follows:

We meet here today in great sorrow. A beloved friend, a wise counselor, is absent. I knew Dr. Begg only slightly before I assumed office as your president, over a year ago, but since then we had been very intimately associated; I became very fond of him, and learned to appreciate his untiring effort and loyalty to the interests of the Society, his great capacity for understanding the capabilities of men, his stern integrity and honesty, and, above all, his keen delight in living this troublesome life of ours. I traveled to Chicago with him less than a week before he died. He contributed much at the meeting in regard to the role of the medical schools in matters of medical preparedness, and appeared in excellent health. On the return trip he left the train at Albany, with the keen expectation of a visit to his new granddaughter, of whom he was very proud. He returned to Boston, settled the affairs of his office, went to bed and slipped quietly into his last sleep. Although we have the deepest sympathy for his children, who in such a short period of time have lost their parents, we should give thanks that he was spared a long and distressing illness.

Alexander Swanson Begg was born in Council Bluffs, Iowa. He attended Collegiate Institute, Sarnia, Ontario, and Drake University. He received his medical degree from Drake University College of Medicine in 1907. From 1907 through 1913 he held successively the positions of instructor, assistant professor and professor of pathology, histology and embryology at Drake University College of Medicine. During 1911 and 1912 he was also a teaching fellow at Harvard Medical School, and in 1913 was appointed instructor in comparative anatomy. Dr. Begg was appointed dean of the graduate medical school at Harvard in 1918. In 1921, after a period as professor of anatomy at Carnegie Institute, he became professor of anatomy at Boston University School of Medicine, and in 1923 was raised to the position of dean of Boston University School of Medicine.

Dr. Begg was a fellow of the American Medical Association and held memberships in the American Association of Anatomists, American Association of Medical Colleges, American Association of University Professors, Association of Military Surgeons and many other organizations.

In 1935 he was elected secretary of the Massachusetts Medical Society, which office he held at the time of his death; he was also Massachusetts chairman of the National Committee on Medical Preparedness of the American Medical Association.

We may indeed say: "Well done, thou good and faithful servant. . . . Enter thou into the joy of thy lord."

All members of the Council rose and stood in silence for a minute.

The President appointed Dr. Robert N. Nye, Suffolk, secretary *pro tempore*, and this was confirmed by vote of the Council.

The records of the annual meeting of May 21, 1940, were presented by the Secretary *pro tempore*, as published in the June 20, 1940, issue of the *New England Journal of Medicine*. No errors or omissions being noted, the Council voted to approve the records as printed.

REPORTS OF STANDING COMMITTEES

Membership

The report (Appendix No. 2), which was presented by the chairman, Dr. G. Colket Caner, Suffolk, recommended that two fellows be allowed to retire, one to resign, one to have his dues remitted, five to change their membership from one district society to another, and one to be deprived of the privileges of fellowship. The Council voted to accept the report and to approve the recommendations.

Financial Planning and Budget

The chairman, Dr. John Homans, Suffolk, presented the report (Appendix No. 3), which contained the recommendation that one hundred and fifty dollars be appropriated for the use of the special committee of the Committee on Public Relations to study tax-supported medical care in Massachusetts. The Council voted to accept the report and to approve the recommendation.

Arrangements

As the chairman, Dr. Edward J. O'Brien, had been called away from the meeting, the Secretary *pro tempore* read the report (Appendix No. 4). It was accepted by the Council.

Ethics and Discipline

The chairman, Dr. Robert L. DeNormandie, Suffolk, stated that there was no regular report; however, a supplementary report (Appendix No. 5) was presented by the senior member of the committee, Dr. Ralph R. Stratton, Middlesex East. The Council voted to accept the report.

Medical Education and Medical Diplomas

The chairman, Dr. John P. Monks, Suffolk, stated that the committee had been instructed to give a report relative to what changes in the by-laws would be required for a shifting of the responsibility of recommending for fellowship the graduates of unapproved and foreign medical schools from the central committee to a district committee. He reported progress and requested permission to postpone the final report until the next meeting of the Council. It was voted to accept the report and to grant permission to delay the final report.

Others

There were no reports from the Committee on Public Health, Committee on State and National Legislation, Committee on Publications, Committee on Medical Defense and the Committee on Permanent Home.

REPORTS OF SPECIAL COMMITTEES

Public Relations

The report of the committee (Appendix No. 6), exclusive of the report of the subcommittee on the medical-costs insurance plan, was read by its secretary, Dr. Elmer S. Bagnall, Essex North. At the suggestion of the President, the first, second and fourth sections of the report were acted on first and accepted by the Council, action on the third section, which dealt with the medical-costs insurance plan, being deferred for the moment. The first and second recommendations were adopted.

Dr. Thomas H. Lanman, Suffolk, chairman of the subcommittee appointed to formulate and present to the Legislature an enabling act to provide for a medical-costs insurance plan, was then asked to give his report.

Dr. Michael A. Tighe, Middlesex North, moved a recess of fifteen minutes to permit the councilors to read the synopsis of the enabling act, copies of which had been distributed. This motion was duly seconded and passed.

The meeting was adjourned for fifteen minutes.

Dr. Lanman then read the synopsis of the proposed act. He pointed out that what he had read was merely a synopsis of the proposed act, which would conform to the five recommendations of the committee that had been approved by the Council at its meeting in June. He added that specific regulations would be contained in the by-laws of the medical-costs insurance corporation that would be formed by the Society by virtue of the enabling act.

Dr. Lanman then briefly commented on the various sections of the act. He said that Section 2,

which specifies that the trustees be appointed with the approval of a recognized medical society, might cause difficulty, but that the committee was unanimous in its belief that any medical-costs insurance corporation should be under the control of the Society. Section 3, he said, would probably be changed, but the intent was to establish units for medical-costs insurance only in those counties in which the practicing physicians favored the plan. He called attention to the addendum, and requested all to read it carefully.

The President opened the matter for general discussion, calling attention to the fact that no action was to be taken by the Council other than to give suggestions as to changes.

In reply to a question by Dr. Sidney M. Saltz, Norfolk, as to why an enabling act was necessary when a non-profit, prepayment, medical-service group was already in operation, Dr. Lanman replied that experience in other states had indicated that any such corporation should, ideally, be under the supervision of the state commissioner of insurance, regardless of whether or not such a provision was necessary from a legal standpoint.

Dr. Reginald Fitz, Suffolk, asked for a definition of the "recognized medical society" under which the control of the corporation would be. Dr. Lanman answered that the only organization conforming to the definition was the Massachusetts Medical Society, where, in the opinion of the committee, the control belonged.

The treasurer, Dr. Charles S. Butler, Suffolk, inquired as to the cost, if any, of such a plan to the Society. Dr. Lanman replied that he did not know, but Dr. Tighe, a member of the subcommittee and vice-chairman of the Committee on Public Relations, said that no expense was involved, other than the money spent by the Society up to the time of the establishment of the corporation. Dr. George L. Schadt, Hampden, asked from whom the five thousand dollars necessary for the granting of authority to do business in any county was to be obtained. Dr. Lanman replied that this section undoubtedly needed minor changes, but that its chief intent was to ensure reliable financing so that a fly-by-night organization could not get started.

At the request of Dr. John W. Bartol, Suffolk, Dr. Lanman gave an outline of the steps in obtaining the New Jersey enabling act and in creating a medical-costs insurance corporation. He said that, because the latter has been functioning only since June, no data are available as to its ultimate success, and that the Medical Society of New Jersey admits that the scheme is experimental and evolutionary.

In reply to the question of Dr. Edward F. Timmins, Suffolk, as to whether legal counsel had approved of the proposed act, Dr. Lanman replied that a member of the firm of Palmer, Dodge, Barstow, Wilkins and Davis, counsel for the Massachusetts Medical Society, had studied it and that although he had not rendered a written opinion he would do so before the act was submitted to the Legislature.

Dr. Richard Dutton, Middlesex East, asked whether a plan of this sort had been conducted elsewhere longer than it had in New Jersey. Dr. Lanman said that the Michigan plan has been in operation longer, but that it was only when the Ford employees became members that any particular interest had been evinced.

Dr. David Cheever, Suffolk, said that Section 8 seemed to be so worded that a non-participating physician rendering emergency treatment would not be reimbursed by the corporation. Dr. Lanman admitted that the section needed rewording, since the intent was to reimburse any duly registered physician who had rendered emergency service.

Dr. Caner questioned the advisability of specifying that 51 per cent of the physicians in any county must be willing to participate in order for the corporation to be allowed to function in that county. Dr. Lanman said that the wording would undoubtedly be changed but that the intent was to permit operation of the plan only in those counties in which there was a demand for the service.

Considerable discussion followed relative to the geographic designation of the units of the proposed corporation. Since the districts of the Society do not conform to county lines, several councilors said that difficulties were sure to arise. Dr. Albert A. Hornor, Suffolk, finally suggested that "section or sections" be substituted for the words "county or counties" in Section 3.

Since there were no further questions, Dr. Bagnall moved that the third section of the report be accepted and that the third recommendation, namely, the endorsement in principle of the outline for medical-costs insurance enabling legislation, be approved. This was seconded, and passed by vote of the Council. The report of the committee as a whole was then accepted by the Council.

Postgraduate Instruction

The report (Appendix No. 7) was presented by the chairman, Dr. Frank R. Ober, Suffolk, and was accepted by vote of the Council.

Convalescent Care

In the absence of the chairman, Dr. T. Duckett Jones, Suffolk, the report of progress (Appendix No. 8) was not read.

Restoration to Fellowship

The reports of the committees previously appointed to consider petitions for restoration to fellowship were accepted, and the recommendations to reinstate the following three fellows were approved by the Council:

Edward J. Kelley, Watertown (Committee: Albert B. Toppan, Pericles Canzanelli and Eugene F. Gorman).

Burton E. Lovesey, Roslindale (Committee: Guy F. Blood, John F. Ford and John J. Elliott).

Louis F. Salerno, East Boston (Committee: Harvey A. Kelly, George H. Schwartz and Raymond B. Parker).

Others

There were no reports from the Committee on Cancer, Committee on Physical Therapy, Committee to Consider Expert Testimony, Committee on Automobile Insurance Claims, Committee on Industrial Health, Committee on Army Medical Library and Museum and Committee to Study Practice of Medicine by Unregistered Persons.

APPOINTMENTS OF COMMITTEES

Dr. Edwin B. Dunphy, Suffolk, and Dr. Henry W. Hudson, Jr., Middlesex South, were appointed members of the Auditing Committee by the President.

The following committees were approved by the Council to consider petitions for restoration to fellowship:

For Edward T. Abrahams, Pittsfield:

Charles T. Leslie, Modestino Criscitiello, Jr., and I. S. F. Dodd.

For Elmer J. Beaulieu, Whitman:

Walter H. Pulsifer, Joseph H. Dunn and Alfred C. Smith.

For Joseph J. Carella, Quincy:

Charles S. Adams, T. Vincent Corsini and Alfred V. Mahoney.

For L. W. Darrah, Northampton:

Justin E. Hayes, Michael E. Cooney and Joseph R. Hobbs.

For Harry J. Hagerty, Worcester:

John H. Hartnett, Peter A. Colberg and Julius I. Tegelberg.

For Morris J. Ritchie, Westfield:

Archibald J. Douglas, Edward S. Smith and Robert M. Marr.

For Kent T. Royal, North Brookfield:

James C. Austin, Milman Pease and Thomas J. O'Boyle.

For Robert V. Schultz, New York City:

Joseph D. Ferrone, Oliver G. Tinkham and M. Fletcher Eades.

For Honoria K. Shine, Holyoke:

Edward P. Bagg, George D. Henderson and Patrick E. Gear.

The President asked for confirmation of the following committee to confer with a similar com-

nittee from the American Hospital Association in regard to various matters, including defense preparedness:

Howard M. Clute, Boston, *chairman*
Benjamin H. Alton, Worcester
Richard B. Cattell, Boston
Edwin D. Gardner, New Bedford
Albert E. Parkhurst, Beverly
Frank W. Snow, Newburyport

The following interim appointments by the President were approved by the Council: Henry C. Marble, Suffolk, chairman of the Committee on State and National Legislation; H. Quimby Gallupe, Middlesex South, and Reginald Fitz, Suffolk, councilors.

INCIDENTAL BUSINESS

The President referred to a suggestion made in his report at the annual meeting of the Society in June, namely, the serious consideration of the advisability of creating the office of president-elect, and asked for comments. Dr. Homans moved that, in view of the fact that a secretary had to be chosen in the near future, the President appoint a committee of five to study the desirability of establishing the offices of president-elect and full-time or executive secretary and the necessary changes in the by-laws required to create these positions. The motion was seconded. After some discussion, chiefly pertaining to a full-time or executive secretary, the motion was passed by the Council.

Dr. Leroy E. Parkins, Suffolk, moved that the remarks of the President relative to Dr. Begg's death be sent to his family as an expression of sympathy and of appreciation of all that he had done for the Society. The motion was seconded and passed.

Dr. Charles E. Mongan, Middlesex South, called attention to the fact that the constitution and by-laws of the Society differ from those of all other state medical societies, which in turn are all modeled after that of the American Medical Association. He said that this applied particularly to the districts of the Society, which in all other states are defined by county lines. He suggested that, since a committee had already been appointed to consider changes in the by-laws, it should also study the propriety of altering the constitution and by-laws in such a way that they would conform to those of other state medical societies, and made a motion to that effect; this was seconded. The Council voted to accept the motion.

Dr. Charles J. Kickham, Norfolk, deplored the fact that the councilors but rarely receive advance

information in regard to matters on which they are supposed to render mature judgment. The President replied that it was the intent of the officers of the Society to inform the councilors in advance, but that one or another factor invariably arose that made such information impossible. He further stated that a more serious effort would be made in the future.

Dr. Harold R. Kurth, secretary of the Essex North District Medical Society, presented a resolution (Appendix No. 9) from that society. He prefaced the reading of the resolution by stating that the physicians in and about Lawrence were concerned by the fact that foreign refugee physicians are permitted to practice in Massachusetts after they have passed the examination of the Board of Registration in Medicine and have signified their intentions of becoming American citizens, as is also true in New York State. He added that most states require full citizenship, and that, as a consequence, these two states are apt to become the concentration point of these foreign-born and foreign-trained physicians. Furthermore, he stated that in certain instances, their conduct is not along strictly ethical lines. He said that this concern had resulted in a petition by the Greater Lawrence Medical Society to the Essex North District Medical Society requesting an opinion and that the latter had rendered its opinion in the form of the resolution that he presented. Considerable discussion followed. Dr. Charles C. Lund, Suffolk, pointed out that two years previously the Committee on State and National Legislation had been instructed by the Council to approve and promote legislation requiring only the first naturalization papers and that a move within such a period of time to demand full citizenship would seriously handicap the committee in its work; he moved that the resolution be referred to the Committee on State and National Legislation. The motion was seconded, and passed by the Council.

In closing the President urged all councilors to return the questionnaires sent out by the Committee on Preparedness of the American Medical Association, and asked them in turn to inform fellow members to do the same. He said that blank questionnaires could be obtained at the headquarters of the Society.

The meeting was adjourned at 1:00 p.m.

ROBERT N. NYE, *Secretary pro tempore*.

APPENDIX NO. 1

ATTENDANCE

BARNSTABLE

M. E. Champion
D. E. Higgins
W. D. Kinney

Frederic Hagler
G. D. Henderson
M. W. Pearson
A. G. Rice
G. L. Schadt

BERKSHIRE

J. J. Boland
I. S. F. Dodd
C. F. Kernan

HAMPSHIRE

A. J. Bonneville
L. N. Durgin
L. B. Pond

BRISTOL NORTH

R. M. Chambers
W. H. Allen
F. H. Dunbar
W. H. Swift

MIDDLESEX EAST

G. R. Murphy
C. R. Baisley
J. H. Blaisdell
Richard Dutton
E. M. Halligan
J. H. Kerrigan
K. L. MacLachlan
R. W. Sheehy
R. R. Stratton

BRISTOL SOUTH

G. W. Blood
R. B. Butler
P. E. Truesdale

ESSEX NORTH

R. C. Norris
E. S. Bagnall
R. V. Baketel
C. S. Benson
E. H. Ganley
H. R. Kurth
P. J. Look
L. C. Peirce
G. L. Richardson
F. W. Snow
T. N. Stone
C. F. Warren
C. A. Weiss

MIDDLESEX NORTH

W. M. Collins
R. L. Drapeau
D. J. Ellison
F. L. Gage
A. R. Gardner
G. A. Leahey
E. O. Tabor
M. A. Tighe

MIDDLESEX SOUTH

Dwight O'Hara
C. F. Atwood
E. W. Barron
Harris Bass
E. H. Bigelow
G. F. H. Bowers
R. W. Buck
E. J. Butler
Richard Collins, Jr.
B. F. Conley
P. A. Consales
D. F. Cummings
C. H. Dalton
H. F. Day
C. L. Derick
J. E. Dodd
A. W. Dudley
E. R. Fleming
H. Q. Gallupe
F. W. Gay
H. G. Giddings
H. W. Godfrey
B. I. Goldberg
W. G. Grandison
A. D. Guthrie
A. A. Levi
A. N. Makechnie
R. A. McCarthy
J. A. McLean
Edward Mellus
J. C. Merriam
C. E. Mongan
J. P. Nelligan

ESSEX SOUTH

Loring Grimes
H. A. Boyle
N. P. Breed
S. E. Golden
P. P. Johnson
J. F. Jordan
B. B. Mansfield
A. E. Parkhurst
W. G. Phippen
Horace Poirier
J. R. Shaughnessy
J. W. Trask
C. F. Twomey

FRANKLIN

F. J. Barnard
A. H. Ellis
W. J. Pelletier
H. G. Stetson

HAMPDEN

F. H. Allen
T. S. Bacon
E. P. Bagg
W. A. R. Chapin
J. L. Chereskin
E. C. Dubois
G. L. Gabler
P. E. Gear

E. J. O'Brien
L. S. Pilcher
E. S. A. Robinson
E. F. Ryan
E. J. Sawyer
M. J. Schlesinger
W. N. Secord
E. F. Sewall
E. W. Small
H. P. Stevens
R. A. Taylor
H. W. Thayer
J. H. Townsend
F. Van Nüys
R. H. Wells
M. W. White
Hovhannes Zovickian

NORFOLK

F. P. McCarthy
F. J. Bailey
J. R. Barry
Carl Bearse
M. I. Berman
F. P. Denny
G. L. Doherty
D. G. Eldridge
H. M. Emmons
J. C. V. Fisher
Susannah Friedman
David Glunts
B. T. Guild
J. B. Hall
Morris Ingall
H. J. Inglis
H. L. Johnson
C. J. Kickham
C. J. E. Kickham
E. L. Kickham
D. L. Lionberger
Charles Malone
F. J. Moran
M. W. O'Connell
Frederick Reis
S. M. Saltz
D. D. Scannell
Nathan Sidel
J. W. Spellman
W. J. Walton
N. A. Welch

NORFOLK SOUTH

C. S. Adams
H. H. A. Blyth

PLYMOUTH

J. E. Brady
A. L. Duncombe
P. B. Kelly
P. H. Leavitt
G. A. Moore
D. W. Pope
W. H. Pulsifer

SUFFOLK

A. A. Hornor
A. W. Allen
J. W. Bartol
W. B. Breed

W. J. Brickley
W. E. Browne
C. S. Butler
G. C. Caner
E. M. Chapman
David Cheever
M. H. Clifford
H. M. Clute
R. L. DeNormandie
N. W. Faxon
G. B. Fenwick
Reginald Fitz
Channing Frothingham
M. N. Fulton
Joseph Garland
John Homans
Rudolph Jacoby
H. A. Kelly
T. H. Lanman
R. I. Lee
C. C. Lund
G. R. Minot
W. J. Mixter
J. P. Monks
Donald Munro
H. L. Musgrave
R. N. Nye
F. R. Ober
J. P. O'Hare
L. E. Parkins
Helen S. Pittman
W. H. Robey
G. C. Shattuck
R. M. Smith
Augustus Thorndike, Jr.
E. F. Timmins
S. N. Vose
Shields Warren
Conrad Wesselhoeft

WORCESTER

J. M. Melick
J. C. Austin
Gordon Berry
W. P. Bowers
G. A. Dix
G. E. Emery
J. M. Fallon
J. J. Goodwin
E. L. Hunt
E. R. Leib
W. F. Lynch
A. W. Marsh
J. C. McCann
J. W. O'Connor
W. C. Seelye
C. A. Sparrow
G. C. Tully
F. H. Washburn
S. B. Woodward

WORCESTER NORTH

B. P. Sweeney
E. A. Adams
H. C. Arey
T. R. Donovan
C. B. Gay
J. C. Hales

APPENDIX NO 2

REPORT OF THE COMMITTEE ON MEMBERSHIP

The committee recommends

1 That the following named two fellows be allowed to retire under the provisions of Chapter I, Section 5, of the by laws

Connell, Arthur I, Fall River
Fales, A C, Wolfville, Nova Scotia

2 That the following named fellow be allowed to resign under the provisions of Chapter I, Sections 6 and 7, of the by laws

LaLiberté, Elie J, Springfield, with remission of dues for 1938, 1939 and 1940

3 That the dues of the following named fellow be remitted under the provisions of Chapter I, Section 6 of the by laws

Jones, Raymond C, Fitchburg, 1940

4 That the following named five fellows be allowed to change their membership from one district society to another without change of legal residence, under the provisions of Chapter III, Section 3, of the by laws

From Middlesex South to Suffolk

Hurxthal, Lewis M, Newton Centre
Ziegler, Edwin L, Brighton

From Norfolk to Suffolk

Birtlett, Marshall K., Dedham
Davis, Lincoln, Needham
Fine, Jacob, Chestnut Hill (Brookline)

5 That the following named fellow be deprived of the privileges of fellowship under the provisions of Chapter I, Section 8 (c) of the by laws

Carogana, Anthony P, Chelsea

G COLKET CANFR *Chairman*

APPENDIX NO 3

COMMITTEE ON FINANCIAL PLANNING AND BUDGET

The Committee on Financial Planning and Budget has been asked by the President to report on the granting of an appropriation of one hundred and fifty dollars for the use of a special committee of the Committee on Public Relations to make a study of tax supported medical care in Massachusetts enlisting the co-operation of state, city and town welfare, old age and veterans' relief administrators, looking toward better standards of care and better mutual understanding of problems of the physicians and of the public agencies. This matter was brought up at the May 1940 meeting of the Council. The committee has voted in favor of this appropriation.

This report therefore carries the following recommendation. That one hundred and fifty dollars be appropriated for the use of a special committee of the Committee on Public Relations for a study of tax supported medical care in Massachusetts enlisting the co-operation of state, city and town welfare, old age and veterans' relief administrators, looking toward better standards of care and better mutual understanding of problems of the physicians and of the public agencies.

JOHN HOMANS *Chairman*

APPENDIX NO 4

COMMITTEE OF ARRANGEMENTS

The committee of Arrangements reports that the annual meeting of the Society will be held on Wednesday and Thursday, May 21 and 22, 1941, at the Copley Plaza Hotel, Boston.

The committee plans to conduct meetings on the same general lines as it did last year. There will be two general clinical meetings on each day, along with round table discussions on the first day.

EDWARD J O BRIEN, *Chairman*

APPENDIX NO 5

SUPPLEMENTARY REPORT OF THE COMMITTEE ON ETHICS AND DISCIPLINE

A special meeting of the Committee on Ethics and Discipline was held on September 18 to consider charges brought against certain members of the Society. The President presided in the absence of the chairman.

After due consideration and lengthy discussion of the evidence presented at that time, it was unanimously decided by the Committee on Ethics and Discipline that the charges were not sustained.

APPENDIX NO 6

REPORT OF THE COMMITTEE ON PUBLIC RELATIONS

The committee has held one meeting since May. The report is divided into four parts.

1 The President appointed the skeleton of a special committee to study certain aspects of tax supported medical care pursuant to authority granted at the Council meeting in May, 1940. This committee reports through the Committee on Public Relations. Bagnall, the chairman, makes the following report of progress.

The special committee appointed by the President on August 6, 1940, to study certain aspects of tax supported medical care has held one meeting. It was decided to ask each district not already represented on the committee to recommend the most interested member in its fellowship for addition to the special committee.

The chairman interviewed Arthur Rotch, commissioner of public welfare for the Commonwealth. The last legislature passed an act authorizing the appointment before September 18, 1940, of an advisory physician for the Department of Public Welfare. The commissioner also is to appoint an advisory committee representing medical, dental and nursing organizations to help solve some of the problems of administration of medical care to the indigent. The committee will not aggressively intrude its studies until it learns what the extent of the state activities will be.

The chairman also interviewed Richard R. Flynn, commissioner of state aid and pensions and learned that there are some practices in the distribution of medical care to veterans that are contrary to the purpose of the law but not actually illegal, for example, the extensive practice of including soldiers' relief and military aid medical service with the work of the city physicians without extra compensation from the department properizes the veterans. Section 17, Chapter 115, in the opinion of the commissioner does not provide free choice of physician but does provide — with

penalty for violation—free choice of druggist, grocer and clothier. The commissioner favors amendment of the law to correct some of these evils.

The Civil-Service Commissioner has been making investigations into alleged fraudulent practice in veterans' medical services in one of the large cities of the Commonwealth for some weeks.

The special committee presents these items as a report of progress.

2. For some months the several members of the Committee on Public Relations have gone to the office of the compensation commissioner of the Works Progress Administration at Boston to see whether federal instructions for "equable distribution of medical service amongst all the physicians in the community qualified and willing to render the service" were being carried out. It has been agreed by each member of the committee that Mr. John F. Burns, the commissioner, was trying to carry out these provisions. There has been notable improvement in the service during the past year, but the committee now believes that more effective scrutiny and closer co-operation can be effected by the appointment of a special committee to take over these monthly inspections.

3. The special committee under the chairmanship of Dr. Lanman presents an outline of proposed enabling legislation to provide medical-costs insurance for physicians' services. The Committee on Public Relations has approved this plan. This bill must be introduced before January 1, 1941, in order to receive the consideration of this session of the legislature. The synopsis is as follows (presented by Dr. Thomas H. Lanman):

TITLE

An act concerning medical service corporations and regulating the establishment, maintenance and operation of medical service corporations and medical service plans.

SECTION 1. This section defines the terms used in the act.

a. A medical service corporation is any corporation organized without capital stock and not for profit, for the purpose of establishing, maintaining and operating non-profit medical-service plans.

b. A non-profit medical-service plan is any plan or arrangement operated by a medical-service corporation, under the provisions of this act, whereby the expense of medical service to subscribers is paid to participating physicians.

c. The terms "subscriber" and "subscriber dependent" are defined in this section.

d. A participating physician is defined as any physician duly licensed to practice medicine in the State of Massachusetts, who agrees in writing with the corporation to perform the medical services specified, at such rates of compensation as shall be determined by the corporation's board of trustees and who further agrees to abide by the by-laws, rules and regulations of the corporation as these relate to participating physicians.

e. Medical service includes all general and special medical services ordinarily provided by such licensed physicians in accordance with the accepted practice in the community at the time the service is rendered.

SECTION 2. This section provides that no person shall be elected a trustee of any medical-service corporation unless his nomination has been approved by a recog-

nized medical society incorporated for not less than ten years and having not less than three thousand members holding licenses to practice medicine in Massachusetts.

SECTION 3. This section provides for the approval of the Commissioner of Insurance. Among other things the certificate of authority which the Commissioner of Insurance will issue to a medical-service corporation shall specify the county or counties in which the corporation is authorized to do business, and no such certificate may be issued unless 51 per cent of the eligible physicians in any county are participating physicians.

SECTION 4. This section provides that no certificate of authority to do business shall be issued to a medical-service corporation by the Commissioner of Insurance unless the corporation holds in cash or bank credits a sum of not less than five thousand dollars.

SECTION 5. This section has to do with contracts. Subscriber contracts shall run for one year. During the first contract year, coverage may be deferred for two months.

SECTION 6. This section further determines all the conditions of the contract entered into by the subscriber.

SECTION 7. Provides the form of contract.

SECTION 8. Relates to participating physicians and provides that no person shall become a participating physician unless he or she shall hold full license to practice medicine in the State of Massachusetts; that no payment for medical services shall be made except to a participating physician, except that the corporation in the case of emergency may reimburse any physician for services rendered to a subscriber in accordance with the rates adopted by the board of trustees with respect to participating physicians, but only to physicians who would be eligible, except for residence, to become participating physicians.

SECTION 9. Provides for the approval of contracts by the Commissioner of Insurance.

SECTION 10. Provides for the approval of rates by the Commissioner of Insurance.

SECTION 12. Provides that not more than 10 per cent of the amounts paid by subscribers in any one year shall be used for the solicitation of subscribers, except that during the first year of the corporation's authority to do business not more than 20 per cent and during the second year not more than 15 per cent shall be used for this purpose.

SECTION 13. This section provides that not more than 20 per cent of the amounts paid by subscribers in any one year shall be used, in any one year, for administrative purposes.

SECTION 14. Provides for the disposal of the corporation's surplus funds.

SECTION 15. Provides that the corporation shall prepare an annual statement.

SECTION 16. Provides for the penalties for not observing Section 15.

SECTION 17. Provides for the examination of the corporation's accounts by the Commissioner of Insurance.

SECTION 18 Provides that the Commissioner of Insurance may assess the corporation for the expense of such examination

SECTION 19 Provides the steps which the Commissioner of Insurance may adopt or cause to be adopted in the event of the insolvency of the corporation

SECTION 20 Provides for the acceptance by the corporation of voluntary grants or gifts these to include possible grants by governmental agencies, for the purpose of providing needy persons with medical services. Funds under such grants shall be kept separate. The income from subscribers or the assets accumulated as a result of payment made by subscribers of the corporation shall not be available for the discharge of the obligations incurred under such grants

SECTION 21 Such medical service corporations shall be free from state, county, town and city taxes

ADDENDUM It will be noted that nothing is said in this act about the income groups to be served under the act. Nothing is said directly about fees to be paid participating physicians. Nothing is said about the cost to subscriber patients. The committee wishes to say that such items do not belong in an enabling act. Such matters will be covered by the bylaws of the corporation once the enabling act has been passed by the Legislature. In the event of the passage of this enabling act, these bylaws, in due course of time will be placed before the Council for action. It is also noted that any and all bylaws of this kind must likewise have the approval of the Commissioner of Insurance.

THOMAS H. LANMAN, *Chairman*

4. The committee again considered the proposal of the Massachusetts Department of Public Health for the extension of the crippled children's program to include first attacks of rheumatic heart disease in indigent children under twelve. The proposal envisions establishment of hospital and home care at Boston, Springfield and Worcester by certain authorized physicians and the Committee on Public Relations has no recommendation to make until the several districts have had a chance to consider the matter. Some districts have had no meeting since the subject was introduced.

The following recommendations are made:

1. That the Committee on State and National Legislation be authorized to introduce amending legislation with the co-operation of the Commissioner of State Aid and Pensions to eliminate the practice prevailing in some localities of providing medical care for soldiers and their dependents by city physicians and further, to provide a free choice of physician—free choice being already available to this group in the matter of grocers, pharmacists and so forth.

2. That the President be authorized to appoint a special committee of five to make monthly inspections at the office of the compensation commissioner of the Work Projects Administration, 600 Washington Street, Boston, to assist in carrying out the regulations which provide for equitable distribution of medical service among all the physicians in the several communities who are qualified and willing to serve.

3. That the outline for medical costs insurance legislation be endorsed in principle.

ELMER S. BAGNALL, *Secretary*

APPENDIX NO 7

REPORT OF THE COMMITTEE ON POSTGRADUATE INSTRUCTION

The committee has completed the curriculum and organized the faculty for the postgraduate extension courses to be given during the academic year 1940-41. These sessions will begin some time this month, notices of meetings will be published in the *Journal*.

Our current budget is \$13,875, of this the Society has appropriated \$1000 and governmental agencies will furnish the balance. Of this sum \$9525 will be used for the postgraduate extension courses and the balance—\$4350—has been appropriated by the United States Public Health Service to aid in starting a traveling medical library for Massachusetts. As soon as the latter service is available, it will be announced in the *Journal*.

The New England Postgraduate Assembly, to be held at Sanders Theatre, Harvard University, on November 13 and 14, has been organized, the program was printed in the *Journal* issue of September 19, 1940. Detailed programs will be mailed to all registered physicians in the sponsoring states in the near future.

The committee reports that the State Department of Public Health and other governmental agencies are co-operating with the committee in a very constructive manner. A final report of these activities will be made at the annual meeting.

FRANK R. OBER, *Chairman*,
LEROY E. PARKINS, *Secretary*

APPENDIX NO 8

REPORT OF THE COMMITTEE ON CONVALESCENT CARE (OF THE HOSPITAL COUNCIL OF BOSTON)

In 1934 Dr. Haven Emerson of New York, in studying the organized facilities for the care of the sick in Boston, stated that convalescent facilities were inadequate. During 1937 the Bureau of Research at the request of the Department of Medical Social Workers undertook a further study of the problem, and recommended that the Hospital Council of Boston be asked to assume responsibility for continued attack upon the problem of adequate convalescent care through the appointment of a committee.

One immediate and definite step which this committee should take would be a central directory of privately operated nursing homes. A special grant was obtained from the Mason Fund and the Committee on Convalescent Care was fortunate to secure Miss Carrie M. Hall, R.N., as the director of the Nursing Home Information Bureau. Miss Hall was especially well equipped for this position in view of her previous position as head of the Training School for Nurses of the Peter Bent Brigham Hospital.

During the fall and winter of 1938-1939 and of 1939-1940 Miss Hall carried on her studies relative to the nursing home situation as it meets the needs for the care of convalescent patients with chronic disease and the aged. The Bureau of Information has been established with Miss Hall as its director. A large number of nursing homes have been investigated and some have been tentatively approved by the Bureau. It has been Miss Hall's conviction that more than 90 per cent of the patients in these nursing homes are chronic and aged and it is her opinion that this causes a depressive atmosphere for the convalescent patient. Medical supervision is lacking there are no occupational or recreational facilities in the majority

of homes, and there is inadequate provision for special diets. In addition, it has become obvious that nurses should have special training and qualifications in order to give constructive nursing care to convalescent patients.

The nursing-home situation is of tremendous importance in the care of the ill in the City of Boston, and because of lack of organized facilities these privately operated nursing homes care for many patients discharged from hospitals. These nursing homes are not licensed except for the care of the aged, and little information concerning each home is available save that secured by Miss Hall's making an actual tour of inspection. One hundred and sixty-eight such homes are at present listed with the Nursing Home Information Bureau. It is increasingly consulted by medical social workers, physicians and others wishing to secure suitable placement for patients needing this type of care.

The Committee on Convalescent Care is of the opinion that the privately operated nursing home does not provide the solution to the problem of convalescent care because of lack of medical supervision, lack of constructive nursing care, lack of knowledge of the principles of therapeutic diets, lack of regulations regarding equipment such as bathroom facilities and so forth, lack of occupation and recreation which might be supplied by the use of occupational therapy, and an atmosphere of depression created by the preponderance of aged persons—more than 90 per cent of the occupants in these homes are aged or chronic.

The committee has therefore reached a negative conclusion regarding some of the facilities at present in use. Member hospitals were asked by the committee whether there were any funds available or obtainable by the hospitals whereby fifteen dollars a week per patient could be paid to a group of selected nursing homes which would agree to give adequate convalescent care. Replies indicated that it would be impossible to secure this amount for the majority of patients needing convalescent care in these private nursing homes.

The question was also raised as to whether the adequate care of the convalescent alone would adequately cover the present problems facing the community, and it was suggested that it would be wise to study the needs of not only the convalescent but the chronic and aged. It was urged that the Committee on Convalescent Care turn its attention to the entire question of placement of patients in these nursing homes from the point of view not only of the hospital administration but also of the medical social workers. It was voted that Miss Hall be requested to work with member hospitals, securing a complete record of discharges referred to medical social service departments for aftercare in order to obtain information as to the number of individuals involved, the types of care requested and the final disposition of each case. With this type of information it would then be possible to define

the problem as to the type of medical care which discharged patients need and the adequacy with which these needs are at present being met.

In pursuance of this decision of the committee, Miss Hall has undertaken such a study and has begun to accumulate a volume of information concerning the disposition of patients from Boston hospitals. A subcommittee composed of Miss Carrie M. Hall, Miss Ida M. Cannon, Dr. Edward L. Young and Dr. T. Duckett Jones made the following recommendations:

For the purpose of this study, the convalescent patient is one between eighteen and sixty-five years of age who has been under hospital care and who needs further medical and nursing care before return to his place in the community. He may be ambulatory or may need temporary bed care. The temporary bed care should not exceed two weeks; the convalescent period should not exceed six weeks. For the purpose of this study, the chronic patient is one between eighteen and sixty-five years of age who has been ill in a hospital and who for a prolonged period is in need of specialized medical and nursing care and supervision.

Data have already been accumulated but not analyzed on the basis of these definitions for a period of three months. Collection of data for a further period of three months will be carried out during the fall months of this year. Following the analysis of this material the committee will be in a much more satisfactory position to define the community-health problems facing the City of Boston not only in the matter of convalescent care but also as concerns the care of the chronic and the aged. Further recommendations will doubtless result from these studies.

T. DUCKETT JONES,
HENRY E. GALLUP,

Representatives of the Massachusetts Medical Society.

APPENDIX NO. 9

RESOLUTION PRESENTED BY THE ESSEX NORTH DISTRICT MEDICAL SOCIETY

WHEREAS, The requirements for registration in medicine in Massachusetts for refugee doctors are far below the standards of the majority of states; and

WHEREAS, There is serious danger of Massachusetts being flooded with refugee doctors because of these lowered standards; therefore, be it

RESOLVED, That the Massachusetts Medical Society take such action as is within its power to initiate legislation which shall require all refugee physicians to be United States citizens before being eligible for registration in medicine.

CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITALANTEMORTEM AND POSTMORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 26441

PRESENTATION OF CASE

First Admission. A forty-four-year-old Italian housewife entered the hospital complaining of swelling of the feet of three weeks' duration.

The patient had been moderately dyspneic on exertion for many years. One year before admission she first noticed a non-radiating, squeezing precordial pain, aggravated by exercise, and relieved by a few minutes' rest. At this same time polyuria (day, 10 to 15; night, 3 to 4) developed, with some urgency and occasional incontinence. Four months before admission she had an attack of severe, knifelike pain of unstated duration in the upper abdomen and afterward noticed that the urine was darker in color. During the two months before admission she developed cramps in the left arm, which occurred on an average of three times a day and lasted for about fifteen minutes. Three weeks before admission the feet and ankles became swollen; this was most noticeable at night, but still present in the morning. In addition she developed a cough with blood-streaked sputum and had occasional slight nosebleeds. These symptoms were accompanied by headaches and nausea.

The past illnesses and family history were irrelevant. She had had seven pregnancies, five of which were miscarriages. Two children were alive and well.

On examination the patient was a flushed, obese woman of Mongoloid appearance with slanting, protruding eyes. The scleras were slightly icteric, the skin dry. The voice was rough and grating, and she complained of photophobia. The teeth were carious, the throat injected. Examination of the heart was negative except for a systolic murmur at the apex; the blood pressure was 135 systolic, 80 diastolic. Increased breath sounds and coarse rhonchi were present in the middle third of the left chest, axilla and back. The abdomen was held in voluntary spasm, but a nodular liver edge was palpable. There was an orange-sized tender mass in the epigastrium, and another tender mass, believed to be spleen, in the left flank. The flanks were dull to percussion, but no definite fluid wave or shifting dullness could be demonstrated. The lower extremities showed varicose

veins and pitting edema to the knees. On vaginal examination there was some pain on moving the cervix, and masses could be felt in the lateral vaults. The fundi showed arteriovenous nicking, but were otherwise normal.

The temperature, pulse and respirations were normal.

Examination of the urine was negative. Examination of the blood showed a red-cell count of 3,120,000 with a hemoglobin of 10 gm. (photo-electric-cell technic), and a white-cell count of 5000 with 72 per cent polymorphonuclears. A blood film showed moderate achromia of the red cells, with some anisocytosis.

The van den Bergh was approximately 1.5 to 2.0 mg. per 100 cc. biphasic, and a bromsulfalein test showed 90 per cent retention of the dye in the serum. Takata-Ara and formol-gel tests were positive. The basal metabolic rate was +26 per cent on admission, but gradually fell to +5 per cent on the day of discharge. A blood Hinton test was negative.

X-ray examination of the chest was negative except for a high diaphragm. The esophagus showed small varices in its lower third. A flat abdominal plate showed a large soft-tissue mass in the left upper quadrant, consistent with a large spleen, which displaced the stomach to the right. The liver shadow appeared smaller than usual.

The patient asked to go home and was discharged on the tenth hospital day.

Second Admission (thirteen months later). In the interval the patient was forced to restrict her activity to light housework and was unable to walk far because of dyspnea. Gradually the abdomen increased in size, ankle edema became more noticeable and the jaundice intensified. In the latter months the urine had become brown, and she suffered from anorexia and cramps in the left leg that were similar to those in the left arm.

The additional findings noted on physical examination were as follows: The skin was light yellow, and the respiratory movements were short and rapid. The tongue was large and thick, the hair fine, but oily. Rales were heard at the lung bases. The abdomen was protuberant, with numerous telangiectases and striae over its surface. The pouting, blue umbilicus overlay a slightly tender hernial opening 4 cm. in diameter. The abdomen was tender throughout, and the liver and spleen were considered to be enlarged. A ballotable mass was present in each upper quadrant, and both extended down to the umbilical line. Shifting dullness was demonstrable. There was pitting edema of the legs and of the sacrum up to the

second lumbar vertebra. Pelvic examination showed an atrophic vagina, with adhesive bands constricting the lumen, and a small cystocele and rectocele. The cervix was small, firm and lacerated; the vaults were clear. Hemorrhoid varices were present.

Examination of the urine showed a + test for bile on two occasions. Examination of the blood was unchanged. The van den Bergh test was 5.8 mg. per 100 cc. biphasic; the bromsulfalein test showed 70 per cent retention, and the formol-gel test was positive. The serum protein was 6.6 gm. per 100 cc., and the uric acid 2.5 mg. The blood calcium was 8.3 mg. per 100 cc., the phosphorus 1.6 mg. and the phosphatase 21.3 units. The bleeding time was 4 minutes, the clotting time 14 minutes.

X-ray studies showed varices in the lower third of the esophagus and a high diaphragm. A Graham test was negative.

An electrocardiogram was within normal limits. During hospitalization the patient ran a spiking temperature up to 100°F., and on the ninth day had a profuse nosebleed that was stopped by adrenalin. She refused abdominal paracentesis and was discharged three weeks after admission, her condition unchanged.

Final Admission (three months later). After discharge the jaundice and edema gradually increased, and the abdomen became more protuberant. She had spent the last four weeks in bed and on the night before admission had had a severe epistaxis that lasted until morning.

On examination the patient was not dyspneic, but respirations were rapid. The skin was dry and deep yellow, and bruises were present on the left cheek and ear. There was pitting edema to the clavicles. Clotted blood was present in the left nostril, and there was evidence of recent bleeding from the gums. The right chest, except at the apex, was flat to percussion, with diminished breath sounds, and a few moist rales were heard at the left lung base. The protuberant abdomen showed a caput medusae and a marked fluid wave. Because of the marked ascites, no organs could be felt. The temperature was 98.8°F., and the pulse 92.

Examination of the urine showed a ++ test for albumin, and a ++++ foam test for bile. Examination of the blood showed a red-cell count of 2,160,000 with a hemoglobin of 50 per cent, and a white-cell count of 19,550 with 90 per cent polymorphonuclears. The serum van den Bergh was 15.7 mg. per 100 cc. biphasic, the nonprotein nitrogen of the blood serum 38 mg., and the

chlorides 93.3 mg. The prothrombin time was 29 seconds (normal 22 seconds), and the cell volume 28.5 per cent. Examination of the stools was negative.

An abdominal paracentesis on the day of admission showed grossly bloody fluid. The procedure was stopped. The patient went rapidly downhill and died on the fifth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. WYMAN RICHARDSON: One year before admission the patient first noticed non-radiating, squeezing precordial pain aggravated by exercise and relieved by a few minutes' rest. Although this is the first symptom recorded, we hear nothing about it in the rest of the report. I must say that after reading the first paragraph I did not want to try to figure out a definite diagnosis. However, after reading the rest of the history and taking a bird's-eye view of the whole thing from first to last, taking care not to get bothered by a lot of discrepancies, one can say that this patient died of liver failure and presumably of cirrhosis of the liver. I do not see why most of the symptoms cannot be explained by ordinary cirrhosis of the liver. I believe that is what this patient had. However, one has to consider, perhaps, one or two other possibilities. In the first place, did she have some sort of malignant tumor? When malignant tumor involves the liver, by the time that it does so sufficiently to give a considerable number of symptoms the progress is very rapidly downhill, and one would therefore not expect a story so long as this. The presence of masses on physical examination brings up the question of some sort of tumor, but the masses seemed to come and go in a manner that leaves one doubtful whether any definite tumor masses were actually palpated. Someone felt a nodular liver. I find it very difficult to determine by palpation through the rectus muscle whether a liver is nodular. Knowing well that primary tumors of the liver usually develop on top of cirrhosis of the liver, and that cancer of the biliary tract usually develops on top of a chronically inflamed gall bladder containing stones, I believe that this patient did not have malignant tumor.

Quite often the question of cardiac cirrhosis is considered. I am always getting confused by it. One should consider the possibility that the patient had had long-standing circulatory failure, as a result of which she developed cirrhosis of the liver. It is my impression that cardiac cirrhosis develops in patients with long-standing failure of the right heart, which is not the case in this patient. The edema began only three weeks before

admission. If it is not cardiac and is evidence of liver failure, it indicates a bad prognosis. The other thing that suggests heart failure is the story of precordial pain. Nothing is said about it except one sentence, and although we are led to believe that she had more than one attack of non-radiating pain we must put that aside in the absence of any further evidence of heart failure. The initial symptom was dyspnea. We know she was obese, which probably accounts for the dyspnea.

Now as to other types of cirrhosis—are we going to differentiate alcoholic from portal cirrhosis? There was no history of alcoholism, and if the patient had cirrhosis, I should say that it is what we ordinarily speak of as portal cirrhosis. We must think also of toxic hepatitis with consequent liver distortion and liver failure. There is no clear-cut attack of acute jaundice, and the history is not suggestive of such a condition. We do, however, have to consider the possibility of some primary liver disease, such as cirrhosis, with terminal evidence of necrosis of the liver. Syphilis of the liver must also be considered. The only thing that suggested it is the history of miscarriages, against it we have the negative blood Hinton test. I am inclined to favor the evidence given by the latter.

Finally, should we consider some condition that causes venous obstruction? Thrombosis of the splenic and portal veins or thrombosis involving venous circulation to such an extent as to produce edema and ascites and also varicosities is a possibility. Nothing in this patient, however, suggests primary thrombosis to me. If we do not go into the history in detail, it is consistent with cirrhosis of the liver in an Italian—and we know that Italians very commonly have cirrhosis of the liver, I should say that this patient had portal cirrhosis of the liver, with a question of terminal necrosis to explain the rapid fatal termination.

I want to speak of two additional findings. One is the question of calcium, phosphorus, and phosphatase. In discussing these cases I have often found it of great advantage not to know too much, and I hope it is going to be an advantage to me now because I cannot explain these rather curious findings of low calcium and low phosphorus. Usually if the calcium is low the phosphorus is correspondingly high, and vice versa. I think one might assume that this patient had digestive disturbances for a long period, and that she had difficulty with the absorption of fat and also, partly as a consequence of that difficulty, with absorption of calcium, in addition she had difficulty, perhaps, in absorbing some of the fat soluble vita-

mins. That might explain a reduced calcium somewhat in the way that it occurs in idiopathic steatorrhea. If x-ray studies of the bones had been taken, they might have shown some definite evidence of osteoporosis, but they would not explain to me a low phosphorus. The low calcium level may also account for the frequent muscular cramps, because it approached what we see in tetany. The phosphatase would ordinarily mean that osteoblastic activity was going on, but there is no reason to believe that such a phenomenon existed in this patient. I believe that the phosphatase determination was suggested to differentiate obstructive from intrahepatic jaundice. Just why the phosphatase is elevated in liver disease I do not know. So much for that, which is little enough.

I considered the other question,—the possibility of gallstones,—because of the knifelike pain earlier in the history. Nothing more is said about it, and I do not believe that this patient had obstructive jaundice with subsequent liver damage. I do not see why it is not a straightforward case of cirrhosis of the liver.

DR TRACY B. MALLORY. I should like to ask Dr. Jones to comment on the phosphatase figures.

DR CHESTER M. JONES. Ivy* recently made the statement that if the phosphatase is moderately high, it shows benign obstruction, very high, obstruction due to cancer. I should think that this was at the edge of being a really high figure. In a large group of cases with jaundice, most of the patients do not have bone lesions but intrahepatic disease, as I have said those who have moderately high phosphatase values are apt to have benign or malignant obstruction, and the ones with very high values almost always have cancer. A high phosphatase level occurs infrequently without any bone involvement, also osteoporosis in chronic jaundice cases. I think the explanation Dr. Richardson gave is as good as any. We can assume that the bile salts are not produced normally, fat absorption is not normal, and therefore there is interference with the absorption of calcium.

DR AUBREY O. HAMPTON. Have you seen a normal Graham test in a patient with varices in the esophagus?

DR JONES. Yes, I think so. Sometimes a nearly normal dye test is present even when there are varices in the esophagus.

DR GEORGE W. HOLMES. This patient has rather typical shadows consistent with varices. Varices usually mean cirrhosis of the liver. Al-

*Ivy and Cowie C. personal communication.

though they may be present as a congenital condition or from thrombosis of the splenic vein, the great majority of our cases have had cirrhosis. It is fairly easy to point out the enlarged mass in the left upper quadrant that was interpreted as being spleen and that in all probability is spleen. We can be sure that the patient had varices and an enlarged spleen. The small liver is not so easily demonstrated. In fact x-ray determination of the size of the liver is never very accurate. Strangely enough one can always see the liver better by fluoroscope than on films, and I should be willing to accept that interpretation. Later on it was said that the liver was large. That interested me. I do not know whether a cirrhotic liver that has once become small can subsequently enlarge. I think we ought to consider more seriously the possibility of malignant tumor.

DR. RICHARDSON: Was the enlargement of the liver an x-ray interpretation?

DR. HOLMES: No, that was clinical.

DR. RICHARDSON: I think that can be disregarded.

DR. HOLMES: Perhaps so. I am giving the clinicians more credit than you are.

DR. MALLORY: It is fair to point out that on both second and third entries the patient had a great deal of ascites. On one occasion she refused to be tapped, and on another the tap was stopped because of hemorrhage. The only physical examination when the abdominal cavity was not full of fluid was therefore the first one.

DR. JONES: Sometime a small liver on top of a lot of ascitic fluid may be readily palpable.

DR. MALLORY: You are not changing your opinion, Dr. Richardson?

DR. RICHARDSON: No.

DR. MALLORY: Does anyone want to disagree with him?

DR. JONES: I should like to consider hepatoma superimposed on a cirrhosis. I see no reason to doubt cirrhosis, but I think one ought to include the distinct possibility of intrahepatic malignant disease.

CLINICAL DIAGNOSES

Cirrhosis of liver.

Generalized anasarca.

DR. RICHARDSON'S DIAGNOSIS

Portal cirrhosis of liver.

ANATOMICAL DIAGNOSES

Primary cancer of the liver, combined type: adenocarcinoma and hepatoma.

Portal cirrhosis of the liver.

Anasarca.

Icterus, marked.

Splenomegaly.

Varices of esophageal and hemorrhoidal veins, venae breviae and veins of lateral abdominal wall.

Umbilical hernia.

Obesity.

PATHOLOGICAL DISCUSSION

DR. MALLORY: The post-mortem examination showed a small liver—1225 gm.—but a very grossly nodular one. I think the nodules could have been felt. The spleen was much enlarged—700 gm. There were very marked esophageal varices. Both the splenic and portal veins were dilated. There was a considerable amount of grossly bloody ascitic fluid, and 1500 cc. of grossly bloody fluid in the right pleural cavity. The peritoneal surfaces, however, were perfectly smooth. Some of the large nodules in the liver were soft and necrotic, and between them were many firm nodules and granules of comparatively small size. The gross appearance was unmistakably that of a primary cancer of the liver. Microscopic examination confirms this diagnosis but shows something that I have never seen before. There are two kinds of primary cancer of the liver—the hepatomas that arise from the liver cells, and the adenocarcinomas that arise from the intrahepatic bile ducts. In this tumor some areas show well-differentiated adenocarcinoma, obviously of the bile-duct type, others show typical hepatoma; one can find single microscopic fields in which both types of cells and transitions from one to the other are visible. So I have to call this a primary cancer of the liver, but I cannot call it a simple hepatoma.

Dr. Richardson's point that one would expect a hepatoma with nodules large enough to be felt to progress more rapidly than this is in accord with our experience in this hospital. Yet we have seen hepatomas in which metastases were found in bones three or four years before the patient died. In this case we found no distant metastases, but a few retroperitoneal nodes showed involvement.

DR. EUGENE R. SULLIVAN: What was the explanation of the bloody fluid in the right pleural cavity?

DR. MALLORY: I should guess that they hit a vein in attempting the abdominal tap, and that the red cells passed through the diaphragm from the abdomen to the pleural cavity. I am convinced that there is a fairly free passage of fluid through the diaphragm in many cases.

CASE 26442

PRESENTATION OF CASE

First Admission. A forty-nine-year-old American housewife entered the hospital complaining of pruritus and jaundice of three weeks' duration.

Approximately eight months before admission the patient became fatigued and nervous, and suffered from insomnia. One month later she developed marked pruritus and a skin rash described as forming "welts," which were most noticeable on the abdomen. These symptoms were soon followed by nausea and vomiting and later by jaundice, clay-colored stools and an increase in the vomiting. She entered another hospital, where a laparotomy was performed. The gall bladder and common duct were said to be normal and contained no stones. The common duct, however, contained practically no bile, but nothing abnormal was noted on passing a probe into the hepatic ducts. Postoperatively the wound drained very little, and the jaundice diminished. Six weeks postoperatively the wound suddenly drained a large amount of bile, and at the same time the stools became normal in color. After this the jaundice disappeared, and the patient gained weight rapidly. She remained well until two months before admission, when weakness, fatigue and pruritus returned. One month later the stools again became clay-colored and the jaundice returned, accompanied by "indigestion" without nausea or vomiting. Within one week normal color returned to the stools, but the jaundice and pruritus increased. During the two weeks before admission she remained in bed a great part of the time suffering from anorexia, chills, fever and sweating, with an intermittent cough and "bile-stained" sputum. The urine became red, and there was burning on micturition. She had lost 23 pounds in the previous seven months. There was no history of excessive alcoholic consumption.

The patient had had the usual childhood diseases. Her mother had died of "gallstones" at fifty-seven.

Examination showed that the patient was well-developed, but had obviously lost weight. The skin was dry and deeply jaundiced, and many acne-like lesions covered with scabs were present over the arms, chest, back and abdomen. Examination of the heart and lungs was negative; the blood pressure was 124 systolic, 66 diastolic. There was a well-healed right paramedian surgical incision in the epigastrium. The liver was not enlarged to percussion, but could be felt two fingerbreadths below the costal margin on deep inspiration. Its firm, smooth edge was acutely tender in the mid-clavicular line. The spleen was just palpable, but

not enlarged to percussion. No other masses were palpable, and there were no signs of peritoneal fluid. Examination of the fundi and nervous system was negative.

The temperature, pulse and respirations were normal.

Examination of the urine showed a + test for albumin, +++ test for bile, and 35 white blood cells per high-power field, with urobilinogen present in dilutions up to 1:170. Examination of the blood showed a red-cell count of 3,750,000 with a hemoglobin of 11.9 gm. (photoelectric-cell technic), and a white-cell count of 6000. The white-cell count remained fairly constant during hospitalization except for two readings of 20,900 and 10,700. A red-cell fragility test was within normal limits, and the reticulocyte count was 0.7 per cent. The hematocrit reading was 34 per cent, and the red-cell volume 8.1 cu. microns. The stools varied from yellow to brown and were guaiac negative. A blood Hinton test was negative. The plasma prothrombin was 89.1 per cent normal, the vitamin C 1.05 mg. per 100 cc., the vitamin A 0.2 units, and the total carotenoids normal.

The patient remained in the hospital for the next seven weeks. Her general condition improved, although the serum van den Bergh varied between 12 and 18 mg. per 100 cc. On duodenal drainage rich lemon-yellow bile was obtained, and the sediment showed casts of bile pigment, a few clumps of bilirubin and occasional crystals of cholesterol. Two weeks after admission the urine was free from bile, but two weeks later the test was +++. One month after admission a peritoneoscopic examination was performed. The liver was found to be grayish-green and relatively smooth, though one observer thought that the surface was slightly irregular. A biopsy specimen was taken, and the pathological examination showed bile stasis and the slightest possible trace of biliary cirrhosis. The sedimentation rate was 1 mm. in 60 minutes, but a week later had risen to 58 mm. Bromsulfalein tests showed 50 per cent, 90 per cent and finally, on the day before discharge, 100 per cent retention of the dye in the serum. A quantitative blood bilirubin was 6.8 mg. per 100 cc. at the time of the last liver-function test. The patient was given four blood transfusions during hospitalization.

Second Admission (one month later). After discharge the patient did not improve to any extent. Weakness and pruritus continued, and although her appetite was fairly good, she had frequent attacks of nausea. In addition she developed a vague right-upper-quadrant abdominal pain and a persistent hard cough with white ropy sputum.

At first the stools had been yellow, then yellow-green, and finally, the week before admission, brown. The urine was usually mahogany colored. Two weeks before admission the abdomen seemed to become more deeply pigmented. She had lost 4 pounds in weight since discharge.

There was little change in the physical examination. The skin was dark yellow, and the liver was palpable 5 cm. below the costal margin. Rales were heard at the lung bases.

Examination of the urine showed a + test for albumin and ++ test for bile, with 100 white blood cells per high-power field. Examination of the blood showed a white-cell count of 13,500 and a red-cell count of 3,770,000, with a sedimentation rate of 57 mm. in one hour and a cell volume of 40.3 per cent. The serum van den Bergh was 10.2 mg. per 100 cc., and the serum protein 5.5 gm. A bromsulfalein test showed 90 per cent retention of the dye, and the prothrombin time was 16 seconds. The stools were brown, contained no fat and were guaiac negative. Duodenal drainage yielded a lemon-yellow material, containing many bilirubin casts in mucus, which was obviously lighter than normal.

X-ray examination of the chest and abdomen was negative.

On the seventh hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. RICHARD H. SWEET: I do not know when I have approached one of these problems with so great a feeling of inadequacy, in spite of the fact that I have spent much time in studying the abstract.

"The patient remained well until two months before admission, when weakness, fatigue and pruritus returned." As I read over the story that statement interested me, because I do not recall seeing a case of obstructive jaundice that produced itching in which the itching preceded the jaundice; but that is what happened in this patient.

Do the x-ray films show anything?

DR. AUBREY O. HAMPTON: I assume that this film was taken to show a stone in the common duct, and it does not show anything. I should not be surprised if a stone were there, however. X-ray study does not rule out stones in the common duct, because we seem to miss most of them. The chest appears normal. The liver and spleen so far as I can tell are not abnormal. Both kidneys are low. The right kidney is lower than the left, and one might assume that it is displaced downward by an enlarged liver.

DR. SWEET: I have made a lot of notes, and by a long and devious route I shall try to lead you to a peculiar conclusion. First, are we dealing with obstructive jaundice? It is obvious that we are, because of the clay-colored stools, the urine and the jaundice. The jaundice was not progressive; it was not complete enough to cause absence of bile from the intestinal tract. It waxed and waned. The stools were sometimes clay colored, sometimes yellow and sometimes brown, back and forth. The jaundice cleared and appeared again. I get the impression from reading the history that it tended to become more persistent and less remittent as the disease progressed. The urine had bile and sometimes no bile, and at times urobilinogen was present, findings which indicate that the obstruction was not complete.

Secondly, is there evidence of obstruction to the common duct? We are forced to conclude that there is not, on the basis of most of the data, although if one reads the history superficially there ought to be a common duct stone. I place a great deal of reliance on the statements made by the surgeon at the first operation: There was a normal gall bladder, a normal common duct, perhaps a little smaller than average, which contained no bile, or very little, no evidence of inflammation, no stones and no edema. This finding of very little bile in the common duct interested me, if it was an accurate observation. The behavior of the wound, I cannot explain. A logical explanation would be that a stone had plugged the common duct again, so that bile had backed up and leaked into the wound and out from the wound six weeks later. However, they did not find a stone or a dilated duct, and there is no record of waxing or waning of the symptoms of obstruction during this period. The duodenal-drainage findings—the cholesterol crystals and the bile-pigment casts—might mean a stone, but I think these might also be found in any case of stasis in the common duct where the bile tends to back up temporarily for any reason.

Is there any evidence against stone in the common duct? I am relying a lot on the first operation. There was no pain until toward the end. Before the last operation there was a dull, vague sort of pain in the right upper quadrant but none of the attacks that one usually associates with common-duct stone, although we all see cases occasionally without any pain whatever.

The loss of weight interests me. I have the impression that it was progressive and did not quite match the coming and going of the other symptoms. At times she had nausea and vomit-

ing, but at times she felt well for a period of several months. The weight loss seems to have continued. Whether or not that means cancer, I do not know.

There is very little evidence to suggest obstruction of the ducts from without, rather than from within—for example, by carcinoma of the pancreas or the ampulla. The obstruction was too variable, for one thing, although one occasionally sees in cancer of the head of the pancreas complete obstruction for a period, followed by bile in the stools from temporary letting up of the obstruction. Still, I do not get the impression that there was any such thing here. There was no palpable gall bladder, for example.

Is there any evidence of obstruction to the major hepatic ducts by stones or by lymph nodes or by a mass in the portal fissure? At the first operation these ducts were probed and were found to be patent. If a stone large enough to cause jaundice existed, the chances are that it would fall down into the common duct at some time or other and become more manifest. Lymph nodes at the portal fissure, lymphoma or some other tumor would tend to cause a more progressive type of jaundice than this. I thought of some queer thing such as aneurysm of the hepatic artery, but I do not see why that also would not cause a progressive type of obstruction. Infection might well account for the intermittent type of obstruction. The waxing and waning of an inflammatory process, with changes in the degree of swelling of the ducts and the amount of mucus secretion, would account for the exacerbations and intermissions. Any of the causes that I have mentioned, if they did not result in a complete obstruction, might therefore lead, because of cholangitis, to intermittent obstruction. I do not see any way to decide whether that was so or not. There is plenty of evidence for cholangitis. The patient had chills, fever and intermission of jaundice, with variation in the degree of swelling and tenderness of the liver. She had a positive biopsy specimen, and the duodenal-drainage findings, as I mentioned before, might go with that picture. There was some indication of liver damage, but the evidence seems largely to be that the liver function kept up quite well except for the bromsulfalein excretion, which was consistently low.

Could this be a case of cholangitis alone—without stone or tumor? In the experience of the surgeon at least, such a case is exceedingly rare. Sometimes we see it from a choledochointerferic fistula with communication between the common duct or the gall bladder and the intestinal tract that allows infection to go through a passage

where there is no valvular action, such as is normally present in the ampulla of Vater. This patient probably had nothing like that.

What about other causes of cholangitis and infection in the small bile ducts? I thought of things like hypertrophic biliary cirrhosis, Hanot's type. I do not know much about it. It is apt to occur in young people, but it may cause all these symptoms.

Intermittent obstruction from a diverticulum of the common duct that filled with something and released itself again is another rare possibility.

As I thought about the case I also wondered if there might be something infiltrating along the biliary ducts,—that is, the lesser ducts in the liver,—such as tuberculosis, miliary tuberculosis of the liver. But the occurrence of miliary tuberculosis of the liver with a negative chest plate seems rather fantastic. The patient's cough seems to be stressed in the history, but the chest plate ruled out any such possibility. Syphilis of the liver seems improbable, because she had a negative blood Hinton test. A further possibility of obstruction to the lesser bile duct system, that is, the radicles within the liver, might be an infiltrating malignant process along the ducts with a superimposed cholangitis. Against that possibility we have the result of the examination of the biopsy specimen, but of course the latter was taken from the very edge of the liver and might not have reached the focus of disease. There was a steady loss in weight. With a cholangitis syndrome, evidence of liver damage,—not very severe,—fatigue, anorexia and so forth, it is rather tempting to say that the patient had cancer.

That brings us down to the question of why the surgeon operated the second time. I do not know why he did. I should guess that he thought he was going to find a stone in the common duct, but think he did not. There were biliary cirrhosis and cholangitis; these were obvious. I should think that there was no surgical or operable lesion. I believe that no stone was present, but there might have been something like primary carcinoma of the bile ducts.

DR. CHESTER M. JONES: I have forgotten how many weeks this patient was in the hospital, but when Dr. Bartlett asked me to see the patient with him, I experienced much the same difficulty that Dr. Sweet did, only it took a good many days instead of a few minutes. Many things came up before we decided to operate. Two things that I thought important enough to be brought out were the curious onset of the disease and the itching before the jaundice. As a rule these symp-

toms mean intrahepatic disease. Not infrequently patients with cirrhosis of any type may have itching before they have any other symptom. The itching consequently made me suspect that the patient had some intrahepatic disease at the beginning and that she might well have had a curious type of catarrhal jaundice or infection of the liver. In retrospect I should still consider that a probability, although no one can prove it. When we examined the patient one other finding, that Dr. Sweet has commented on several times, was that she became more and more jaundiced, although the stools contained bile. I have been impressed with that as an important criterion against operation. To me it means intrahepatic disease unless one has clear evidence of partial obstruction of the duct. As a rule, surgery is contraindicated in such cases. Deep jaundice associated with brown stools must mean serious damage to the liver, although it may be transient. It was on that basis that I believed, and Dr. Bartlett was of the same opinion, that operation should be deferred. We sent the patient home with instructions to return if she did not get better. She did not improve and returned, stating that she had had clay-colored stools for several days prior to the re-entry. The second duodenal drainage showed less bile than the first. On that basis we decided to operate. I believed that there were two possibilities: trauma to the common duct at the time of the first operation and a stenosing cholangitis.

DR. SWEET: I did not consider the question of trauma produced at the first operation because she had the same type of symptoms before both operations.

DR. MARSHALL K. BARTLETT: Dr. Jones has very well summed up our reasons for operating. There were, of course, adhesions around the gall bladder. When freed, the gall bladder was a little thickened, and contained a small amount of dark-brown bile. We exposed the common duct, which was considerably dilated to a point just below the entrance to the cystic duct. From there on it was normal in size. We opened it and found a good deal of bile under pressure and a constriction just below the point where the cystic duct came in. A plastic procedure seemed indicated and was carried out.

DR. JONES: I should like to add that Dr. Bartlett deserves credit for adhering to his impression that he would eventually be forced to operate.

DR. BARTLETT: We operated because the prognosis seemed unfavorable if it was hepatic disease; we also thought that there was a slight but real possibility that something might have occurred at the first operation that could be corrected.

CLINICAL DIAGNOSIS

Stricture of common duct?
Stenosing cholangitis?

DR. SWEET'S DIAGNOSES

Biliary cirrhosis.
Recurrent acute and subacute cholangitis.
A stenosing process in the biliary radicles, possibly carcinomatous.

ANATOMICAL DIAGNOSES

Traumatic stricture of the common duct.
Intrahepatic bile stasis.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: I was asked to see this patient on the ward and I am afraid my reaction is evidence that the pathologist's mind works in dark and devious ways. I could not explain the picture satisfactorily on any natural cause, so I immediately suspected the surgeon. At that time I wrote: "Review of this patient's history, biased perhaps by having previously examined a fragment of her liver microscopically, inclines me to put as my first choice in diagnosis a partial traumatic stricture of the common duct, rather than primary hepatic disease."

Dr. Bartlett took a second biopsy specimen of the liver at the time of his operation; this showed the same picture as the earlier one, namely, changes characteristic of prolonged biliary obstruction. There had been no detectable progression of the lesion in the interval.

The patient made a rapid convalescence and is now, several months later, apparently completely well. Needless to say the development of the stricture reflects no discredit on the first surgeon. It is a complication, fortunately a rare one, which may follow any exploration of the common duct.

The New England Journal of Medicine

Formerly the
Boston Medical and Surgical Journal
Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE
ON PUBLICATIONS

Official Organ of
THE MASSACHUSETTS MEDICAL SOCIETY
THE NEW HAMPSHIRE MEDICAL SOCIETY
THE VERMONT STATE MEDICAL SOCIETY

EDITORIAL BOARD

Joseph Garland M.D.	John P. Sutherland M.D.
William B. Breed M.D.	Stephen Rushmore M.D.
George R. Minot M.D.	Henry R. Viets M.D.
Frank H. Lahey M.D.	Robert M. Green M.D.
Sheldon Warren M.D.	Charles C. Lund M.D.
George L. Tobey Jr. M.D.	John P. Fulton M.D.
C. Guy Lane M.D.	A. Warren Stearns M.D.
William A. Rogers M.D.	Dwight O'Hara M.D.

ASSOCIATE EDITORS

Thomas H. Lanman M.D.	Donald Munro M.D.
Henry Jackson Jr. M.D.	
Walter P. Bowers M.D.	EDITOR EMERITUS
Robert N. Nye M.D.	MANAGING EDITOR
Clara D. Davies	ASSISTANT EDITOR

SUBSCRIPTION TERMS \$6.00 per year in advance postage paid for the
United States Canada \$ 04 per year \$2.52 per year for all foreign coun-
tries belonging to the Postal Union

MATERIAL for early publication should be received not later than noon
on Saturday

THE JOURNAL does not hold itself responsible for statements made by any
contributor

COMMUNICATIONS should be addressed to the *New England Journal of
Medicine* 8 Fenway Boston Massachusetts

SELECTIVE SERVICE REGISTRANTS AND VENEREAL DISEASE PREVENTION

THE recent agreement between the War Department, the Navy Department, the Federal Security Agency and state health departments for the control of venereal diseases, which appears in this issue of the *Journal*, recalls the great disability caused in World War I by these diseases—the third highest cause of disability. More than 6,500,000 man-days were lost to the army because of these infections, and about 350,000 of officers and men were treated. This was a tremendous waste, and much of it could have been avoided if the communities in which these infections occurred had had proper venereal disease control measures and had enforced them.

Proper planning now will do much to prevent a repetition in the present crisis of the experiences

of the last war. The 16,500,000 registrants in this first peacetime draft constitute the age group in which are concentrated most of the infectious cases of syphilis and gonorrhea, and the United States Public Health Service will provide each of the registrants with a leaflet containing facts about these diseases and their relation to national defense, urging that each have a blood test for syphilis as a part of an initial check on physical fitness. Blood tests of this group will contribute to the discovery of a large number of cases of syphilis in the stage of the disease in which treatment is most effective, and such treatment will result in bringing nearer by many years the control of syphilis in the whole population, as well as benefiting the individual registrant. The immediate discovery and treatment of syphilis among registrants will increase the reservoir of men available for active and efficient duty both in the armed forces and in industry. If, in addition to the examination and blood testing of registrants, there is an adequate control of venereal disease in areas where armed forces and national defense employees are concentrated, there should be a marked reduction in the number of new infections.

This educational and control program, sponsored by the United States Public Health Service, in co-operation with state and local health authorities, together with the aid of physicians everywhere, will, as Assistant Surgeon General Vonderlehr states, "contribute substantially to the physical fitness of men in the armed and industrial defense forces" and will help this country to benefit tremendously by the lessons of the last world war.

TRICHINOSIS AGAIN

THE United States Public Health Service is continuing to emphasize the past and present incidence of trichinosis, and to indicate where control measures against the disease are most likely to be effective. The *Journal* has not infrequently commented on this problem in public health, and pointed out that it is as formidable here in New England as it is anywhere else. Many local physicians first learned to recognize prevalence of trichi-

nosis in the period between 1920 and 1930, and yet Dr. Henry I. Bowditch¹ wrote in 1877: "I would suggest the same doubt about trichiniasis being a new disease as about cerebrospinal meningitis; because there is no doubt, from morbid specimens existing in European cabinets, that trichiniasis existed many years ago, without being recognized in the complete manner which it is at the present day." Why this disease became so generally overlooked or disregarded during the next half century is not easy to understand.

Human trichinosis comes from eating uncooked or inadequately cooked pork. Swine trichinosis arises primarily from feeding uncooked garbage containing pork scraps, either from tables or markets, to the pigs. The direct method of prevention would therefore be either to cook the garbage or to keep the pork scraps out of it before allowing it to be used as pig food. It is hard to refrain from any opportunity to revile the common rat, and one might also appease his sanitary conscience by casting some aspersion on the filthiness of many pigsties; the nucleus of the problem, however, concerns itself with the use of uncooked garbage in the swine industry. In many cities and towns the only improvements effected in the methods of garbage disposal have concerned themselves with designs for garbage trucks. One may freely admit the degree of progress manifested in a comparison of the old-fashioned swill wagon with the modern streamline self-hoisting tanks, but when they get to their ultimate destinations, "pigs is pigs," and they still get trichinosis.

In a recent issue of *Public Health Reports*, Wright² reports the result of a survey of seven hundred and sixty-four cities of 10,000 population or over. Of the four hundred and three cities that responded, only twenty-four indicated that all or a part of the garbage was cooked before being fed to swine. The New England states lead all other geographic areas in the number of cities using the hog-feeding method of garbage disposal, and consequently they have, as a group, the next to the highest morbidity rate for the disease. Because many hogs, maintained on municipal gar-

bage of this sort, are slaughtered and consumed locally, it is probable that many cities maintain within their own borders the vicious circle that continues the disease among their citizens.

The Bureau of Animal Industry, of the United States Department of Agriculture, has no jurisdiction over products which do not cross interstate lines, although it does much in an advisory and supervisory way. Hence, proper conduct of the local swine industry remains a challenge to the administrators of our towns and cities. Local government used to be at its best in New England!

REFERENCES

1. Bowditch, H. I.: *Public Hygiene in America*. 498 pp. Boston: Little, Brown and Company, 1877. P. 96.
2. Wright, W. H.: A survey of municipal garbage disposal methods as related to the spread of trichinosis. XIV. Studies on trichinosis. *Pub. Health Rep.* 55:1069-1077, 1940.

MEDICAL EPONYM

ERB'S PARALYSIS

"Ueber eine eigenthümliche Localisation von Lähmungen im Plexus brachialis [A Peculiar Localization of Paralysis in the Brachial Plexus]" was discussed by Professor Wilhelm Heinrich Erb (1840-1921) before the Society of Natural History and Medicine at Heidelberg on November 10, 1874, and published in the *Verhandlungen des Naturhistorisch-Medicinischen Vereins zu Heidelberg* (Neue Folge 1:130-136, 1877). A portion of the translation follows:

On looking through my case histories of peripheral paralysis, I have found a number of cases of paralysis of the upper extremity, which were marked by a striking correspondence and grouping of the muscles involved. . . . These paralyzes were *not* localized in any one main trunk of the brachial plexus, but rather involved certain muscles, always the same ones, which are innervated by the various branches (with the exception of the ulnar nerve) of the plexus. . . . It would seem . . . that the lesion . . . is located in the fifth or sixth cervical nerves (or their anterior branches) or perhaps at their point of junction. . . . A further category of similar cases is formed by certain types of the obstetric paralyzes which are not very uncommon in the newborn. . . . It seems probable . . . that the use of the so-called Prague grip which is usually necessary in version and extraction is the commonest cause of this special form of "obstetric paralysis." The fingers, grasping the neck like a fork, may, if the obstetrician's procedure is somewhat energetic, so compress the roots or the plexus itself that a more or less stubborn paralysis results.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS
AND GYNECOLOGY*

RAYMOND S. TITUS, M.D., *Secretary*
330 Dartmouth Street
Boston

PREMATURE LABOR AND DELIVERY
IN A DIABETIC PATIENT

Mrs. M.B., a twenty-one year-old primipara, was first seen in the office on April 12, 1932, when she was approximately five months pregnant.

The family history was non-contributory. The patient's past history included scarlet fever and chicken pox. She had undergone an appendectomy and a tonsillectomy. Diabetes was discovered in 1931 and was controlled by 28 units of insulin daily. Catamenia began at eleven, were regular with a twenty-eight day cycle and lasted four to five days. The last normal period began on October 27, 1931, making the expected date of confinement August 3.

Physical examination revealed a well-developed and well-nourished young woman. The weight was 129 pounds, a gain of 9 pounds since the summer. The heart was not enlarged, there were no murmurs. The lungs were clear and resonant, there were no rales. The blood pressure was 100 systolic, 54 diastolic. Abdominal examination revealed the fundus to be 23 cm. above the symphysis, the position of the fetus was not determined. The fetal heart was heard. Vaginal examination showed the cervix to be soft.

During the remaining months of pregnancy the patient was seen frequently by the obstetrician and a specialist in diabetes. The insulin dosage was increased to control the diabetes. A blood sugar test on May 31 showed 200 mg. per 100 cc., and another on June 23 showed 140 mg.

On June 30 the patient was seen in the office. At this time the fundus was 31.5 cm. above the symphysis. The fetal heart was heard. The patient's weight was 144 pounds, and the blood pressure 110 systolic, 60 diastolic.

On July 7, when the patient was approximately thirty-six weeks pregnant, she entered the hospital in desultory labor. A vaginal examination on admission revealed that the cervix was dilated sufficiently to admit two fingers, was not entirely taken up, and was stiff. Contractions continued off and on throughout the day, and on July 8 by a simple forceps operation the patient was delivered

of an 8½ pound male infant. The convalescence was entirely uneventful.

At the time of final examination, on August 19, the patient was sugar free. The weight was 111 pounds, the blood pressure was 112 systolic, 64 diastolic, and pelvic examination was negative.

Comment. Mild diabetic patients frequently start premature labor spontaneously; few go to term. Although this patient was only thirty-six weeks pregnant, the baby weighed 8½ pounds. She has since had a second baby, also born one month early, which was likewise the fat, edematous infant usually delivered by diabetic patients.

MEDICAL POSTGRADUATE
EXTENSION COURSES

The following sessions, given by the Massachusetts Medical Society in co-operation with the Massachusetts Department of Public Health, the United States Public Health Service and the Federal Children's Bureau, have been arranged for the week beginning November 4.

BARNSTABLE

Sunday, November 10, at 4 00 p.m., at the Cape Cod Hospital, Hyannis. Chemotherapy in the Treatment of Gonococcal Infection. Instructor Oscar F. Cox. Donald E. Higgins, *Chairman*.

BRISTOL NORTH

Thursday, November 7, at 4 00 p.m., at the Morton Hospital, Taunton. Pediatric Case Discussions. Instructor Harold L. Higgins. Lester E. Butler, *Chairman*.

BRISTOL SOUTH (New Bedford Section)

Friday, November 8, at 4 00 p.m., at St. Luke's Hospital, New Bedford. The Clinical Recognition of the Types of Jaundice and Recent Advances in Their Treatment. Instructor Franz Ingelfinger. Robert H. Goodwin, *Chairman*.

ESSEX NORTH

Friday, November 8, at 4 30 p.m., at the Clover Hill Hospital, Lawrence. Management of Abdominal Distention. Instructor Jacob Fine. John Parr, *Chairman*.

ESSEX SOUTH

Tuesday, November 5, at 4 00 p.m., in the Conference Room, Salem Hospital, Salem. Technique and Treatment of Primary, Secondary and Tertiary Syphilis. Instructor C. Guy Lane. J. Robert Slaughnessy, *Chairman*.

MIDDLESEX NORTH

Friday, November 8, at 5 00 p.m., at St. John's Hospital, Lowell. Problems in Bronchoscopy. Instructor Lyman G. Richards. William S. Lawler, *Chairman*.

PLYMOUTH

Tuesday, November 5, at 4 30 p.m., in the Nurses Home of the Brockton Hospital, Brockton. Chemotherapy in the Treatment of Gonococcal Infection. Instructor P. N. Papas. Walter H. Pulsifer, *Chairman*.

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

MISCELLANY

MEASURES FOR THE CONTROL OF THE VENEREAL DISEASES IN AREAS WHERE ARMED FORCES OR NATIONAL DEFENSE EMPLOYEES ARE CONCENTRATED

The following agreement was adopted by the Conference of State and Territorial Health Officers in May, 1940, and has since been approved by the Secretary of War, the Secretary of the Navy and the Administrator of the Federal Security Agency:

It is recognized that the following services should be developed by state and local health and police authorities in co-operation with the Medical Corps of the United States Army, the Bureau of Medicine and Surgery of the United States Navy, the United States Public Health Service and interested voluntary organizations:

1. Early diagnosis and adequate treatment by the Army and the Navy of enlisted personnel infected with venereal diseases.

2. Early diagnosis and treatment of the civilian population by the local health department.

3. When authentic information can be obtained as to the probable source of venereal-disease infection of military or naval personnel, the facts will be reported by medical officers of the Army or Navy to the state or local health authorities as may be required (familial contact with naval patients will not be reported). If additional authentic information is available as to extramarital contacts with diseased military or naval personnel during the communicable stage, this should also be reported.

4. All contacts of enlisted men with infected civilians to be reported to the medical officers in charge of the Army and Navy by the local or state health authorities.

5. Recalcitrant infected persons with communicable syphilis or gonorrhea to be forcibly isolated during the period of communicability; in civilian populations, it is the duty of the local health authorities to obtain the assistance of the local police authorities in enforcing such isolation.

6. Decrease so far as possible the opportunities for contacts with infected persons. The local police departments are responsible for the repression of commercialized and clandestine prostitution. The local health departments, the state health departments, the Public Health Service, the Army and the Navy will co-operate with the local police authorities in repressing prostitution.

7. An aggressive program of education both among enlisted personnel and the civilian population regarding the dangers of the venereal diseases, the methods for preventing these infections, and the steps which should be taken if a person suspects that he is infected.

8. The local police and health authorities, the state health departments, the Public Health Service, the Army and the Navy desire the assistance of representatives of the American Social Hygiene Association or affiliated social hygiene societies or other voluntary welfare organizations or groups in developing and stimulating public support for the above measures.

CORRESPONDENCE

DEPRIVATION OF LICENSES

To the Editor: The license of Dr. John A. Carter, of Highland Avenue, Malden, Massachusetts, was revoked by the Board of Registration in Medicine on October 15 because of conviction in court of abortion, and that of Dr. Maurice Goldberg, 12 Market Square, Amesbury, Massachusetts, was suspended for the period of one month because of participation in the production of termination of pregnancy.

STEPHEN RUSHMORE, M.D., *Secretary,*
Board of Registration in Medicine

State House,
Boston.

NOTICES

ANNOUNCEMENT

LESTER S. KAHN, M.D., announces the opening of an office at 1673 Beacon Street, Brookline. He is retaining his office at 416 Marlboro Street, Boston.

BOSTON DOCTORS' SYMPHONY ORCHESTRA



The Boston Doctors' Symphony Orchestra will rehearse under Alexander Thiede, former concertmaster with the Cleveland Symphony Orchestra, every Thursday at 8:30 p.m. Those interested in becoming members should com-

municate with Dr. Julius Loman, Pelham Hall Hotel, Brookline (BEA 2430).

BOSTON SOCIETY OF BIOLOGISTS

The next meeting of the Boston Society of Biologists will be held at the Biological Laboratories, Divinity Avenue, Cambridge, on Wednesday, November 20, at 8:00 p.m.

PROGRAM

- Observations on the Brown-Pearce Carcinoma in Roller Tile Tissue Cultures. Dr. Francis S. Cheever.
- Growth and Differentiation in Plant Tissue Cultures. Dr. Folke Skoog.
- Metabolism of Tissues Grown in Culture. Drs. Austin M. Brues and Hildegard Wilson.
- Inhibition of Growth in Vitro. Drs. Austin M. Brues and Joseph C. Aub.

WILLIAM HARVEY SOCIETY

The second lecture of the series sponsored by the Tufts College Medical School's William Harvey Society, "Experimental Studies in Pernicious Anemia: With particular reference to the changes in the nervous system," will be given by Dr. Maxwell M. Wintrobe, of Baltimore, in the auditorium of the Beth Israel Hospital, Boston, on Friday, November 8, at 8:00 p.m. Dr. William Dameshek, assistant professor of medicine at Tufts, will be chairman of the meeting.

PETER BENT BRIGHAM HOSPITAL

A joint medical and surgical clinic at the Peter Bent Brigham Hospital will be held on Wednesday, November 6, from 2 00 to 4 00 p m Drs Joseph C Aub and Francis C Newton will speak, their subject being 'Obesity'. A clinicopathological conference, conducted by Dr Elliott C Cutler, will take place from 4 00 to 5 00 p m Physicians and students are cordially invited to attend

NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held in the classroom of the nurses' residence on Thursday, November 7, at 7 15 p m The subject 'Clinical Allergy' will be considered Dr Eda A Polcari will preside as chairman

NEISSERIAN MEDICAL SOCIETY OF MASSACHUSETTS

The Neisserian Medical Society of Massachusetts will hold a dinner meeting in the Marine Room, Hotel Kenmore, Boston, on Wednesday, November 13, at 7 00 p m

PROGRAM

Dinner (\$2 25).

Election of officers

Report of the 1940 meeting of the American Neisserian Medical Society

Gonorrhea and National Defense Dr P S Pelouze, of Philadelphia

Five minute reports from various members on activities in their respective communities

All interested persons are cordially invited to attend

NEW ENGLAND SOCIETY OF ANESTHESIOLOGY

The November meeting of the New England Society of Anesthesiology will be held at the Boston City Hospital on Tuesday, November 12, at 8 00 p m Dr Albert Miller, of Providence, Rhode Island, will speak, his subject being 'Mechanics of Gas Anesthesia'

The December meeting will be held at the Massachusetts General Hospital on Tuesday, December 10, at 8 00 p m Dr M J Nicholson will speak on 'Fractional Spinal Anesthesia'

POSTGRADUATE COURSE IN OBSTETRICS

The Department of Obstetrics and Gynecology of the University of Chicago and the Chicago Lying in Hospital through the co-operation of the Children's Bureau, United States Department of Labor and the Illinois State Department of Public Health offers five postgraduate courses in obstetrics of four weeks each between January 6 and June 21. The beginning dates of each are January 6, February 10, March 17, April 21 and May 26. All the members of the department and all services and units of the institution participate in the instruction. Only a limited number of postgraduate students are accepted for each period. A deposit of \$25 00 is required, of which \$10 00 is returned on completion of the course. All communications should be addressed to Postgraduate Course, 5848 Drexel Avenue, Chicago, Illinois

UNITED STATES NAVAL HOSPITAL

A change has been made in the program of medical meetings to be held at the United States Naval Hospital in

Chelsea. The meeting scheduled for November 14 has been changed to November 13, and the subject will be 'A Trip Through the Gastrointestinal Tract with the Fluoroscope' by Dr Merrill C. Sosman.

SOCIETY MEETINGS AND CONFERENCES**CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING SUNDAY, NOVEMBER 3****MONDAY NOVEMBER 4**

12 15-1 15 p m Clinicopathological conference Peter Bent Brigham Hospital amphitheater

TUESDAY NOVEMBER 5

*9-10 a m Management of Pulmonary Abscess Dr R H Ellis Joseph H Pratt Diagnostic Hospital

12 15-1 15 p m Clinicoradiological conference Peter Bent Brigham Hospital amphitheater

WEDNESDAY, NOVEMBER 6

*9-10 a m Hospital case presentation Dr S J Thannhauser Joseph H Pratt Diagnostic Hospital

*12 m Clinicopathological conference Children's Hospital

*2-4 p m Obesity Drs J C Aub and F C Newton Peter Bent Brigham Hospital

THURSDAY NOVEMBER 7

*8 30 a m Combined clinic of the medical surgical orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital at the Children's Hospital

*9-10 a m Carcinoma of the Pancreas Clinical review of cases Dr E P Engleman Joseph H Pratt Diagnostic Hospital

7 15 p m Clinical Allergy Monthly clinical conference and meeting of staff New England Hospital for Women and Children

FRIDAY NOVEMBER 8

Society for Research in Child Development Harvard Medical School

*9-10 a m Experimental Studies in Pernicious Anemia Dr Maxwell M Wintröbe Joseph H Pratt Diagnostic Hospital

8 p m Experimental Studies in Pernicious Anemia Dr Wintröbe William Harvey Society Auditorium Beth Israel Hospital

*8 15 p m New England Heart Association Boston Medical Library 8 Fenway

SATURDAY NOVEMBER 9

Society for Research in Child Development Harvard Medical School and Children's Hospital

*9-10 a m Hospital case presentation Dr S J Thannhauser Joseph H Pratt Diagnostic Hospital

*Open to the medical profession

NOVEMBER 8 15 and 22—Thomas William Salmon Memorial Lectures Page 692 issue of October 24

NOVEMBER 12—New England Society of Anesthesiology Notice above.

NOVEMBER 13—Neisserian Medical Society of Massachusetts Notice above

NOVEMBER 13—United States Naval Hospital Notice above

NOVEMBER 13 14—New England Postgraduate Assembly Cambridge Massachusetts

NOVEMBER 14—Pentucket Association of Physicians Page 263 issue of August 15

NOVEMBER 14—American Conference on Industrial Health Page 648 issue of October 17

NOVEMBER 15—Massachusetts Society for Mental Hygiene Page 645 issue of October 17

NOVEMBER 20—Boston Society of Biologists Page 742

DECEMBER 10—New England Society of Anesthesiology Notice above

DECEMBER 27-29—National Convention of the Association of Medical Students Boston

JANUARY 4 1941—American Board of Obstetrics and Gynecology Page 1064 issue of June 20

MAY 8—American Board of Ophthalmology Page 201 issue of August 1

APRIL 21-23—American College of Physicians Page 1065 issue of June 20

MAY 21 22—Massachusetts Medical Society Boston

JUNE 2-6—American Medical Association Cleveland Ohio

DISTRICT MEDICAL SOCIETIES**FRANKLIN**

NOVEMBER 12

JANUARY 14

MARCH 11.

MAY 13.

Meetings will be held at 11 a.m. at the Franklin County Hospital, Greenfield.

SUPFOLK

NOVEMBER 7 — Censors' meeting. Page 305, issue of August 22.

JANUARY 29 — Page 604, issue of October 10.

APRIL 30 — Page 604, issue of October 10.

WORCESTER

NOVEMBER 13 — Grafton State Hospital, Grafton.

DECEMBER 11 — St. Vincent Hospital, Worcester.

JANUARY 8, 1941 — Worcester City Hospital, Worcester.

FEBRUARY 12 — Worcester State Hospital, Worcester.

MARCH 12 — Memorial Hospital, Worcester.

APRIL 9 — Hahnemann Hospital, Worcester.

Supper at 6:30 p.m. followed by a business meeting and scientific program.

BOOK REVIEWS

Introduction to Medicine. By Don C. Sutton, M.D., with introduction by Ada Belle McCleery. 8°, cloth, 642 pp., with 144 text illustrations and 14 color plates. St. Louis: C. V. Mosby Company, 1940. \$3.25.

There are a number of difficulties in writing a textbook of medicine for nurses. The question of elimination of a large amount of material, the simplification of the language, the emphasis on diagnostic tests with which the nurse must be familiar and the particular attention that must be given to drug therapy make a book of this type different from the ordinary text for medical students. The author has succeeded in evaluating his material and has produced a book which should be of interest to nurses.

Most of the illustrations, however, are poor, and there are too many dealing with physical diagnosis. Most of them were taken from a book written by the same author under that title. The type is larger than necessary, the paper is poor and in general the book presents a shabby appearance. It cannot be highly recommended.

Clinical Parasitology. By Charles Franklin Craig, M.D., M.A. (Hon.), and Ernest Carroll Faust, M.A., Ph.D. Second edition, thoroughly revised. 8°, cloth, 772 pp., with 244 illustrations. Philadelphia: Lea & Febiger, 1940. \$8.50.

This volume is devoted to a systematic treatment of the animal parasites of man. While primary emphasis is placed on the morphology and biology of the parasites, symptoms, therapy and prophylaxis are also considered.

The material is divided into sections on the protozoa, helminths (including leeches) and arthropods. A helpful technical appendix which gives methods of cultivation and preservation of the parasites, an extended summary of the international rules of zoological nomenclature and a twenty-six page bibliography are included.

The style is clear and positive; the presentation of controversial material is reduced to a minimum. The numerous illustrations, both originals and copies, are well chosen and well reproduced, and considerably aid the textual explanation.

The special competence of the authors in the fields of protozoology and helminthology makes these sections noteworthy. The account of the history and synonymy of *Plasmodium ovale* is most interesting. The opinion concerning the sarcosporidia, namely, that "it is likely that further investigation will show that the latter are also fungi," is not likely to win universal acceptance nor is the other opinion that the complement-deviation test in amebiasis constitutes one of the "more important landmarks in the development of human parasitology." The

helminthologist will note the account of the life of *Strongyloides stercoralis*, including the description of a parasitic male.

The revised text has been very carefully assembled, and the inevitable errors seem extremely few. Present evidence does not warrant the statement, "Neither of these agents [chloramine and chlorine] can be employed to render water safe that is contaminated with the cysts of this parasite [*Entamoeba histolytica*]." The translation of "lagochilascaris" as "hare-beaked" seems not more accurate and less illuminating than "hare-lipped," since the lips are a characteristic of this genus.

The book is designed primarily for the physician and the student of medical parasitology. The reviewer has no hesitation in recommending it as one of the most useful of the modern texts on the subject written in English.

The Patient's Dilemma: The quest for medical security in America. By Hugh Cabot, M.D. 8°, cloth, 284 pp. New York: Reynal & Hitchcock, 1940. \$2.50.

The Patient's Dilemma is not a heavy scientific work but rather, as the author confesses, a philosophical expression of "the faith that is in me." One might expect from the former professor of surgery and dean of the University of Michigan Medical School and consultant and teacher at the Mayo Clinic a book replete with the wisdom gained of long medical experience, to which, in addition, rare character and ethical insight had been brought. But other men equally competent in medicine have not shown the corresponding grasp of economic and social theory so amply demonstrated in this book.

The book opens with a brief survey of the revolution in modern medical practice as a consequence of the impact of recent scientific discoveries, goes on to define the elements of good medical care, estimates its cost, argues ably for the superior quality and lower cost of group practice and outlines a conservative but progressive plan for getting good medical service to the majority of the population.

The author is convinced that the role of charity must decline, that government co-operation and intervention under the guidance of medical experts must increase if security in this field is to be made general. He is anxious that, in any program to be adopted, public opinion should be represented as well as government, physicians, scientists, hospital administrators and so forth. Many of the old shibboleths of conservatives in medicine are refuted here. Dr. Hugh Cabot is familiar with all the stock arguments against government intervention, weighs them judiciously and objectively and leaves the reader distinctly with the impression that, in Dr. Cabot's opinion, while there are difficulties to be overcome, they are not insurmountable. With many of his arguments and proposals a large number of physicians will disagree.

The evidence of need the author reviews well. The problem, according to him, is how to meet it before a combination of pressure groups and unwise politicians bungles the job and prevents the enactment of an effective plan that will not only give good medical service to all but will protect the professional interests of physicians.

Had the book been written a few months later, Dr. Cabot might well have been led to stress the urgency of adopting a program which would furnish good medical service to all in the interest of national strength and defense. For it seems axiomatic that no amount of wealth or maturity of industrial power, can save a nation in the days of international conflict if the health of its manpower is anything less than optimum.

The New England Journal of Medicine

Copyright 1940 by the Massachusetts Medical Society

VOLUME 223

NOVEMBER 7, 1940

NUMBER 19

INSULIN RESISTANCE*

Report of a Case

JAMES F. REGAN, MD,† J. JOHN WESTRA, MD,‡ AND RUSSELL M. WILDER, MD§

ROCHESTER, MINNESOTA

THE knowledge that by the intelligent use of insulin combined with dietary regulation almost all cases of diabetes mellitus can be satisfactorily controlled affords the physician considerable peace of mind. However, it is important to remember that the fundamental metabolic defect in this disease is still a subject of controversy, and that since the discovery of insulin little has been learned of the mechanism by which it effects the oxidation of dextrose. This fact is forcibly brought to one's attention when one encounters a patient who exhibits the phenomenon variously designated as "insulin resistance" and as "insulin antagonism." The consensus is that the former term may be used when a patient requires more insulin than the clinical character of his disease seems to demand, especially when amounts in excess of 100 or 150 units are taken daily for considerable periods without insulin reactions, or without obtaining the expected effect on the blood sugar or glycosuria. In most cases of diabetes when the patient requires between 100 and 150 units, a responsible complication can almost invariably be disclosed, and even so, the total daily dose rarely exceeds 150 units. When larger dosages are required, or when the explanation available for high requirements is inadequate, the condition is properly called "insulin resistance."

CASE REPORT

A 53-year-old accountant who lived in Alaska registered at the Mayo Clinic on August 12, 1938, complaining of a slight loss of weight, an occasional tired feeling and periodic polydipsia and polyuria. His father had died of diabetes mellitus at the age of 78.

In July, 1937, the patient had an attack of influenza and was confined to bed for 2 or 3 days because of fever, weakness, nausea, vomiting and sharp pain in the pit of

the stomach. He recovered shortly but felt worn out. Two weeks later he had a similar attack and remained in bed for 10 days. At his own suggestion a urinalysis was performed and the presence of diabetes mellitus was discovered. He was placed on a diet and went for treatment to Seattle, where, after a complete examination, he was placed on a diet of 200 gm. of carbohydrate, 80 gm. of protein and 100 gm. of fat, and instructed to take 30 units of insulin daily (protamine insulin, 20 units, regular insulin, 10 units). For several months the symptoms were allayed but he made no gain in weight. Although the food was weighed, the patient often failed to fulfill his dietary requirements.

He performed his own urinalyses four times daily, and in January, 1938, again noted sugar in the urine. At this time he began to feel weakness, particularly in the lower part of the back, this was associated with pain. At times he was unable to climb stairs. In February, 1938, a physician discontinued the use of the Joslin diet, placed him on a low-carbohydrate, high fat diet, and increased the daily dose of insulin to 45 units (protamine insulin, 30 units, regular insulin, 15 units), but sugar still persisted in the urine. The patient remained on the diet but gradually increased the dosage of insulin until during the first week in August, 1938, he was taking 96 units per day (protamine insulin, 64 units, regular insulin, 32 units). Despite the large amounts of insulin taken, he excreted sugar in the urine continuously for 8 months. Two weeks before coming to the clinic he returned to the Joslin diet. For 6 months he had no major illnesses, colds or other symptoms, but he became progressively weaker and lost 16 pounds.

During the preceding 10 years he had had several attacks of indigestion. In August, 1937, he had an attack of pain in the right side of the epigastrium. The distress did not disappear as it had before, but persisted for a week and was associated with nausea and vomiting. There was no history of jaundice or intolerance to fatty foods. In July, 1938, five teeth were removed. For a few months before the patient came to the clinic he was somewhat dyspneic on exertion. The appetite was good.

On physical examination the patient appeared thin, emaciated and ill. His height was 69 inches (175.3 cm.), and his weight 132 pounds. His normal weight was 148 pounds, and he had weighed 175 pounds 2 years previously. The skin was dry and somewhat xerotic. The eyes, ears, nose and throat were essentially normal. There was evidence of recent extraction of teeth. The heart and lungs were normal. The abdomen was scaphoid. There

*From the Division of Medicine, The Mayo Clinic.

†Fellow in surgery, The Mayo Foundation.

‡Fellow in medicine, The Mayo Foundation.

§Chief of Department of Medicine and Professor of medicine, The Mayo Foundation, Graduate School, University of Minnesota.

were no palpable masses. The prostate gland was somewhat enlarged. There were marked varicosities in both legs, with some pigmentation on the shins. The peripheral arteries were moderately thickened and tortuous; their pulsations were good. The reflexes were normal.

Because the patient's urine contained acetone and diacetic acid, he was sent to the hospital, where the examination was completed. The concentration of hemoglobin and the red-cell count were normal. The white-cell count was 5000. The sedimentation rate was normal—7 mm. at the end of 1 hour. Roentgenologic examination of the thorax disclosed no abnormality, and a roentgenogram of the gall bladder revealed a non-functioning organ. The results of the Kline, Kahn, Hinton and Kolmer tests on the blood serum were negative. Dental examination revealed

quirement rose rapidly, until it was necessary to give 300 units daily; even then, marked glycosuria was present.

There was very little local reaction at the site of injection of the insulin. However, insulin was given intravenously for 6 days. The requirement continued to rise steadily under this regime (Fig. 1).

The concentration of chlorides was 617 mg. per 100 cc. of plasma; the value for the sodium was 311 mg. per 100 cc. of serum, and that for the potassium was 20 mg. per 100 cc. Although the concentration of plasma chlorides approached the upper normal limit, large amounts of sodium chloride were given, since the procedure had previously been found helpful in some cases of insulin resistance.¹ Two thousand cubic centimeters of a 2 per cent solution of sodium chloride was given daily

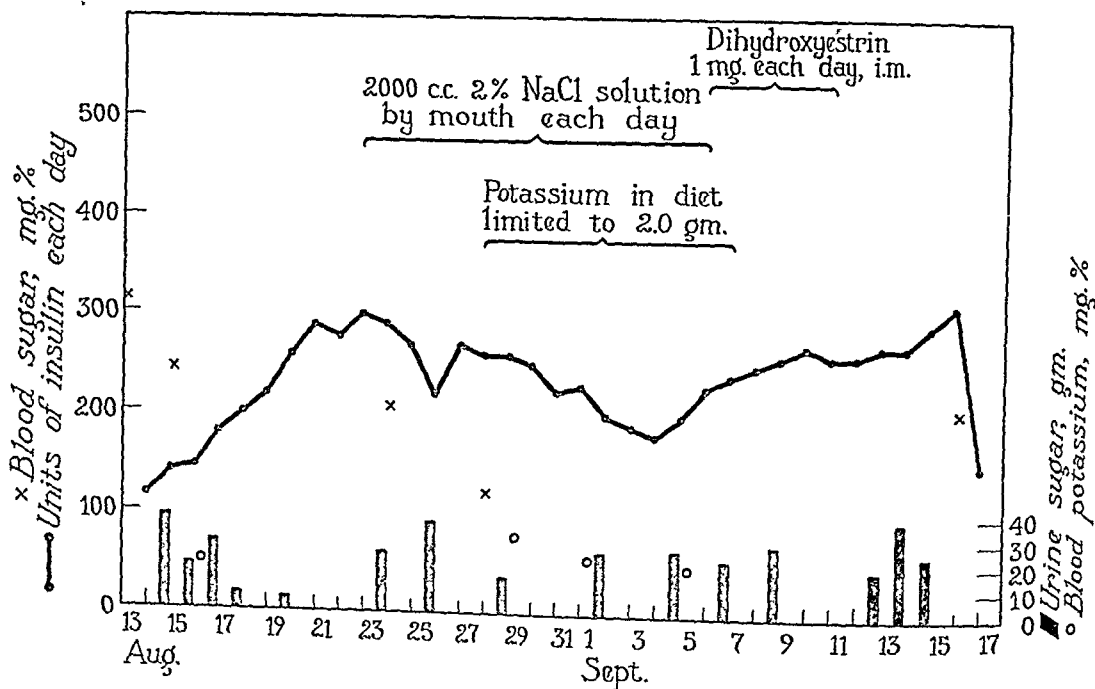


FIGURE 1. *Insulin Requirements in a Case of Insulin Resistance, and the Effect Thereon of Administration of Sodium and Potassium.*

moderate periapical infection and pyorrhea. Removal of the upper second molar tooth on the right side was advised. Examination of the ear, nose and throat revealed moderate septal deflection. The tonsils showed minimal evidence of infection. The pupils reacted promptly to light and accommodation. The ocular fundi appeared normal. There was no evidence of infection of the prostate gland. The basal metabolic rate on different days was -9 and -3 per cent. The liver-function test revealed no retention of the dye. The concentration of serum bilirubin was 1.0 mg. per 100 cc., and the van den Bergh reaction was indirect. The electrocardiogram showed sinus arrhythmia and low amplitude of T waves in Leads 2 and 3. Examination of a biopsied section of skin disclosed no evidence of hemochromatosis.

On admission to the hospital the patient was placed on a standard diabetic diet, which consisted of 147 gm. of carbohydrate, 75 gm. of protein and 147 gm. of fat. The value for the fasting blood sugar the next morning was 306 mg. per 100 cc., and the carbon dioxide combining power of the plasma was 59.8 vol. per cent. The patient continued to excrete large amounts of sugar in the urine, with traces of acetone and diacetic acid. The insulin re-

quirement rose rapidly, until it was necessary to give 300 units daily; even then, marked glycosuria was present. It was then decided to place the patient on a diet low in potassium, that is, one that supplied from 1.2 to 2.0 gm. of potassium daily. As shown in Figure 1, the insulin requirement fell to 180 units in 7 days and then began to rise. On August 29, 1938, the concentration of potassium was 31 mg. per 100 cc. On the low-potassium diet the concentration of serum potassium fell. On September 1 it was 22 mg. per 100 cc. and on September 5 20 mg.

Large doses of female sex hormone—10,000 units of dihydroxyestrin—were given intramuscularly for 4 days. The insulin requirement, however, continued to rise.

There seemed to be no explanation for the insulin resistance except a possible pancreatitis secondary to chronic cholecystitis, which was indicated by the history and the roentgenologic report of a non-functioning gall bladder. No lipase was present in the serum. There were 106 units of amylase in each 100 cc. of serum. However, cholecystectomy was advised.

On September 15 a cholecystectomy and an exploratory choledochostomy were performed. Manual examination

of the pancreas failed to reveal any abnormality, and there seemed to be practically no induration of the pancreas. The liver showed a slight degree of hepatitis, as evidenced by some rounding of the edge and slight scarring in the region near the fundus of the gall bladder. The common bile duct was about three times the normal size, and in order to be sure nothing abnormal was present to afford prolonged drainage of the biliary tract, a small longitudinal incision was made in it. A small quantity of clear bile and a few bits of flaky material escaped. The pathologists' report was as follows: Gall bladder chronic chole-

stomach. Two thousand cubic centimeters of a 0.9 per cent solution of sodium chloride containing 200 units of insulin was given intravenously. At 8 a.m. the value for the blood sugar was 572 mg per 100 cc and the carbon dioxide combining power of the plasma 12.6 vol per cent. At 11 a.m. the concentration of blood sugar was 600 mg, and the carbon dioxide combining power of the plasma 10.7 vol. The patient was then given 500 cc. of a 5 per cent solution of sodium bicarbonate intravenously and placed on a regime of 100 units of insulin per hour. Respirations became less rapid, and the pain in the epigastrium diminished. The patient became much clearer mentally and was given another 500 cc. of a 5 per cent solution of sodium bicarbonate during the afternoon. At 7 p.m. the value for the blood sugar was 353 mg, and the carbon dioxide combining power of the plasma 32.4 vol. At 2 a.m. the next day (the 5th day after operation) urinalysis disclosed moderate glycosuria, and only a trace of acetone. The dose of insulin was then decreased to 40 units per hour. At 8 a.m. the concentration of blood sugar had decreased to 22 mg and the carbon dioxide combining power of the plasma had increased to 61.7 vol. The patient was drowsy and unable to drink. He was

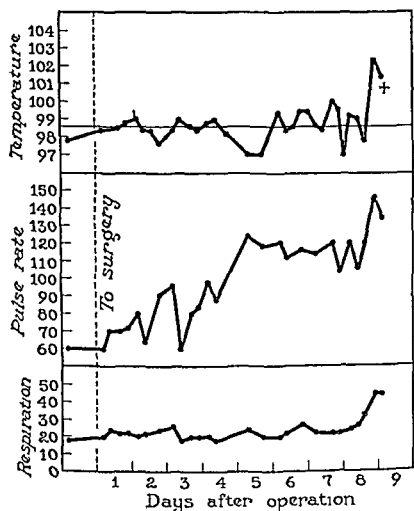


FIGURE 2 Temperature, Pulse and Respirations after Operation in a Case of Insulin Resistance

cystitis with thickened and slightly infiltrated walls, cholelithiasis, multiple stones (largest 15 cm, smallest 30 mm), Regional lymph node inflammatory. A culture taken from the gall bladder revealed a few gram negative bacilli.

Following operation the patient got along very well for the first 3 days. The temperature did not exceed 99°F, the pulse rate did not go above 96, and the respirations remained about normal (Fig 2). The daily insulin requirement gradually rose to 300 units (Fig 3). On the 4th day after operation urinalysis revealed a marked glycosuria, and considerable acetone and diacetic acid. The skin was dry, and there was an acetone odor to the breath. Since the patient had not eaten much, 2000 cc of a 5 per cent solution of dextrose was given intravenously, along with 20 units of insulin. The concentration of blood sugar was 298 mg per 100 cc. During the night he became irrational, vomited several times and complained of pain in the epigastrium. The next morning respirations were rapid, the mouth was dry and the breath had the odor of acetone. At this time the concentration of the blood sugar was 492 mg per 100 cc and the carbon dioxide combining power of the plasma 15.5 vol per cent. Gastric lavage was employed, and 100 cc. of a 5 per cent solution of sodium bicarbonate was left in the

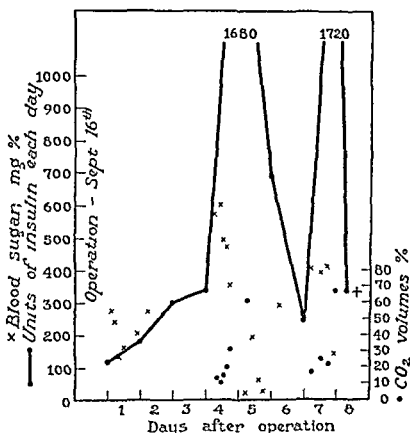


FIGURE 3 Insulin Requirement after Operation in a Case of Insulin Resistance

given 20 cc of a 50 per cent solution of dextrose intravenously, and this was followed by the intravenous administration of 1000 cc of a 5 per cent solution of dextrose in physiologic saline solution. The patient then felt much better.

At 11 a.m. of the 5th day after operation, the value for the blood sugar was 197 mg. One hundred and sixty units of insulin was given at 1 p.m. At 4 p.m. the concentration of the blood sugar was 63 mg. The dose of insulin was decreased from 100 to 50 units and was administered every 3 hours. The patient became rather drowsy and thirsty. At 9 p.m. the value for the blood sugar was 26 mg, and 20 cc of a 50 per cent solution of dextrose was given intravenously. The urine was free of sugar. The dose of insulin was then decreased from 50 to 25 units and was repeated every 3 hours. The urine remained free of sugar during the night. At 8 a.m. of the 6th

day after operation the value for the blood sugar was 291 mg. and urinalysis disclosed a moderately severe glycosuria and traces of acetone and diacetic acid. The patient gradually went into acidosis in spite of increasing doses of insulin. At 8 a.m. of the 7th day after operation the carbon dioxide combining power of the plasma was 17.4 vol. per cent. The skin was dry and respirations were of the Kussmaul type. A total of 1720 units of insulin was given, along with 1500 cc. of a 5 per cent solution of sodium bicarbonate and 3500 cc. of a 0.9 per cent solution of sodium chloride intravenously. At 11:30 p.m. the patient seemed to be in surprisingly good condition, rational and able to take fluids. The concentration of the blood sugar was 140 mg., and the carbon dioxide combining power of the plasma was 67 vol. At 12:30 a.m. of the 8th day after operation the patient's condition suddenly changed. Respirations became of the Cheyne-Stokes type; the systolic blood pressure ranged from 78 to 84, the diastolic from 52 to 56 mm. The pulse rate ranged from 148 to 160; the pulse was thready, and there was great variation in the strength of the beats. The patient soon became irrational. Dextrose and Ringer's solution were administered intravenously, but the blood pressure continued to fall. The patient died at 5:30 a.m.

Necropsy revealed recent bilateral bronchopneumonia with several small recent abscesses in the right lung. There was a moderate degree of generalized atherosclerosis. The common bile duct was twice the normal size. Its wall was thickened, there was evidence of subacute inflammation in the mucosa, and some inflammatory cells were present in the surrounding tissue. The liver was normal in color and consistence, and was not enlarged; on microscopic examination it appeared normal. The pancreas appeared grossly normal. Microscopic examination revealed an occasional abnormal-looking island of Langerhans in the head, and hyalinization of the islands in the tail. There was a small fetal adenoma in the left lobe of the thyroid gland. The thymus had been almost completely replaced by fat. The suprarenal glands, testes, kidneys, prostate gland and pituitary body appeared normal on both gross and microscopic examinations.

COMMENT

Cases of extreme resistance to insulin such as this are fortunately unusual. By far the most spectacular is one reported by Wiener.² The patient, a man aged fifty-eight years, required as much as 3250 units of insulin in twenty-four hours. Wiener made attempts to determine the presence of a contrainsular hormone by injecting the patient's serum into rabbits and noting the effect on the concentration of blood sugar, but the results were negative.

Glen and Eaton³ report a case of diabetes in which the patient, a woman, aged forty-six, required from 900 to 1050 units of insulin daily for twenty-seven days without appreciable effect on the blood sugar or the glycosuria. Her diabetes had begun eight years previously, following the removal of the uterus and an ovary. The insulin requirement rose gradually from the onset of the disease until her death in coma. Glycosuria, thirst and pruritus persisted in spite of the increasing dose, although there was practically no ketonuria.

The basal metabolic rate varied from +49 to +16 per cent during the last two years of her illness, yet there was no clinical evidence of hyperthyroidism. When insulin was given with dextrose, the dextrose tolerance was less than when no insulin was given. When the administration of insulin was stopped, ketosis rapidly developed. The injection of dihydroxyestrin increased the dextrose tolerance and also relieved the pruritus. The parenteral administration of phosphates lowered the concentration of blood sugar for a short time. The injection of the patient's serum along with insulin into rabbits markedly diminished the hypoglycemia produced by insulin. This effect was still more marked if the patient had received insulin before the serum was withdrawn.

Watson and Dick⁴ in 1933 described an experiment that indicated the presence of a substance in the urine of diabetic patients that causes partial inactivation of insulin.

De Wesselow and Griffiths⁵ report that the injection of blood plasma of some elderly, obese glycosuric patients into rabbits diminished the hypoglycemic action of insulin. The plasma of young diabetic patients gave negative results.

Fitz⁶ suggests that some agent is present in the blood and tissues that, in a more direct way than has been suggested, may oppose or neutralize the action of insulin, or that some enzyme needed for activation of insulin, such as an insulin kinase, is deficient because of a defect of the pancreas or liver.

Greene and Thatcher⁷ recently reported a case of resistance to protamine-zinc insulin without resistance to regular insulin. The patient was a woman, aged twenty-seven, who had had diabetes for eleven years. Her diabetes was easily controlled with regular insulin, but when she was placed on protamine-zinc insulin, acidosis and severe glycosuria developed. On intradermal injection of protamine-zinc insulin there was a positive reaction, whereas regular insulin gave none. There were no masses beneath the skin at the site of injection. The authors expressed the opinion that an allergic reaction, as evidenced by the positive skin response, altered the protamine-zinc insulin and thereby prevented it from breaking down and liberating the insulin in the usual manner.

Beamer and Eadie⁸ report that insulin fails to lower the blood sugar in most of their animals (rabbits) poisoned with diphtheria toxin. This resistance to insulin may be annulled by the injection of ergotoxin.

The following conditions have at times been as-

sociated with an increased requirement for insulin: destructive processes in the pancreas, with limitation of insulin-producing tissue, as in cancer, hemochromatosis, multiple calculi and acute pancreatitis; other endocrine disturbances, such as hyperthyroidism and pituitary and adrenal dysfunction; infection; disturbances of function of the liver, as in cirrhosis, chronic passive congestion, hemochromatosis and syphilis; disturbances of function of the skin and muscles, owing to complicating disease, poor development or disuse; cardiac complications with decompensation, edema and shock or circulatory collapse; diabetic acidosis and coma; and damage to the brain stem.

It must be emphasized that most of these disturbances have relatively little effect on the requirement for insulin. Occasionally some of them, such as hemochromatosis, have been associated with great resistance to insulin.

In the case that we have reported we were unable to find any definite reason for the large amounts of insulin required for control of the diabetes prior to operation. As stated, necropsy revealed abnormal-looking islands of Langerhans in the head of the pancreas, and hyalinization of the islands in the tail of the organ. This, however, is a common finding, not only in the pancreas of diabetic patients but in the pancreas of persons who die with no diabetes. It cannot explain the resistance to insulin. The liver, testes, pituitary body and suprarenal glands were normal on gross and microscopic examinations. Normal blood pressure and absence of signs of Cushing's syndrome tended to rule out dysfunction of the suprarenal glands. A small adenoma was present in the left lobe of the thyroid. There was, however, no evidence of hyperthyroidism clinically, and the basal metabolic rate was -9 and -3 per cent on two occasions. It is true that the patient had had intermittent distress in the right upper quadrant of the abdomen for about ten years, and that there was roentgenologic evidence of a non-functioning gall bladder. However, the sedimentation rate was only 7 mm. at the end of one hour, the white-cell count was only 5000, and there was no elevation in temperature. The wall of the gall bladder was thickened and slightly infiltrated. The evidence in favor of infection as the cause of the unusual requirement for insulin seems inconclusive; that present in the lungs was in the nature of a terminal development.

It is interesting to note that although the patient was excreting some sugar in the urine, it was only after he was placed on a low-carbohydrate, high-fat diet that the requirement for insulin began to rise

steadily and continued to do so until the day he was operated on. That this may have contributed to the increased requirement is possible but improbable. All the diets used in the treatment of diabetes in the clinic were relatively low in carbohydrate until recently, yet this is only the second or third case among many thousands in which there has developed such a degree of insulin resistance.

Weakness caused by inadequate caloric intake—the patient was overly cautious and did not eat his full diet—resulted in curtailment of muscular activity. As Smith and Smith⁹ have shown, exercise diminishes hyperglycemia following ingestion of food in normal subjects and in cases of controlled diabetes, but fails to do so in cases of uncontrolled diabetes. This decrease in amount of activity perhaps played a role in the increased insulin requirement in this case, but that it did so to any great extent is most unlikely, to judge from other experiences.

Harrop and Benedict¹⁰ many years ago demonstrated that insulin retarded the excretion of potassium. At the time we were treating this patient, Kendall¹¹ reported the results of experiments on partially depancreatized rats. Following the ingestion of potassium chloride there was a marked increase in the amount of glucose excreted. This seemed to give support to his thesis that the amount of potassium retained in the body might influence the conversion of glycogen and protein to glucose. On the basis of his observation, we placed the patient on a diet containing only 1.2 to 2.0 gm. of potassium per day. The concentration of potassium in the serum fell from an abnormally high value of 31 mg. per 100 cc. to a normal value of 20 mg. on the ninth day of the diet, and the requirement for insulin fell in seven days from 260 to 180 units. However, the requirement then began to rise (Fig. 1).

In 1933, Barnes, Regan and Nelson¹² reported the amelioration of experimental diabetes in dogs following the prolonged injection of female sex hormone. This experiment was repeated later on monkeys by Nelson and Overholser.¹³ On the basis of their observations, 10,000 units of dihydroxyestrin was injected daily for five days without effect. The requirement for insulin even rose for four days; however, no conclusions can be drawn from this, because the injections may not have been continued for a sufficiently long period.

The only conclusion justifiable from the report of this and other similar cases is that nothing is now known that will satisfactorily explain insulin resistance. Some antagonist to insulin that is not present when the treatment is begun must develop

in the course of continuous treatment, because at the beginning the patients do not show this resistance. However, the nature of the antagonist remains obscure. The condition seems to be analogous to the development of insensitivity to parathyroid hormone after it has been given for several weeks to patients with parathyroid tetany, although the latter is much more regular. Also possibly related is Collip's¹⁴ observation of so-called "antibody formation" after long-continued administration of extracts of the anterior lobe of the pituitary body, notably with the thyrotropic hormone. The activity of the hormones of the parathyroid glands and anterior pituitary body apparently depends on the integrity of a basic unit the size of a molecule of protein, which therefore probably possesses antigenic properties. The same is true of insulin. The molecular weight of crystalline insulin as determined by Sjögren and Svedberg¹⁵ is 35,100—almost identical with the values obtained for egg albumen and Bence-Jones protein. These investigators expressed the opinion that insulin is a well-defined protein and that the physiologic activity of the hormone is a property of the insulin molecule itself or of some special group within it. Insensitivity to hormones of simpler chemical structure, such as estrin and thyroxine, has not been reported. That encountered with hormones of the complexity of proteins may depend on antibody-like substances in the blood or, when circulating antibodies are not demonstrable, as in most of these cases, on a type of immunity reaction which, as has been suggested by the work of Gordon, Kleinberg and Charipper,¹⁶ may be limited to fixed tissue cells, such as those of the reticuloendothelial system.

SUMMARY

A case of insulin resistance is reported in which no definite cause for the resistance was found. Necropsy disclosed only terminal bronchopneumonia and recent abscesses of the right lung. Large amounts of sodium chloride were given, with only slight temporary improvement. The

concentration of potassium in the serum was abnormally high; on a low-potassium diet it decreased to normal, and the requirement for insulin decreased temporarily. Administration of dihydroxyestrin did not seem to affect the requirement.

Conditions are mentioned that have at times been associated with diminished sensitivity to insulin. None of them were apparently involved in this case.

Nothing is now known that will satisfactorily explain insensitivity to insulin of the high degree encountered in cases like the one reported. Some antagonist that develops during the course of treatment is involved, and the suggestion is advanced that, owing to the protein nature of insulin, insensitivity to it may result from a type of immunity reaction limited to fixed-tissue cells, such as those of the reticuloendothelial system.

REFERENCES

1. Wilder, R. M., and Wilbur, D. C.: Diseases of metabolism and nutrition: review of certain recent contributions. *Arch. Int. Med.* 59:329-364, 1937.
2. Wiener, H. J.: Diabetic coma requiring an unprecedented amount of insulin: report of a case manifesting extreme insulin resistance. *Am. J. M. Sc.* 196:211-217, 1938.
3. Glen, A., and Eaton, J. C.: Insulin antagonism. *Quart. J. Med.* 7:271-291, 1938.
4. Watson, E. M., and Dick, W. S.: Some observations concerning a possible insulin-inhibiting substance in urine. *Ann. Int. Med.* 6:1171-1179, 1933.
5. De Wesselow, O. L. V., and Griffiths, W. J.: On the possible role of the anterior pituitary in human diabetes. *Lancet* 1:991-994, 1935.
6. Fitz, R.: Does diabetic blood contain an insulin-inactivating substance? *Medical Papers Dedicated to Henry A. Christian*. 1000 pp. Baltimore: Waverly Press, Inc., 1936. Pp. 446-449.
7. Greene, J. A., and Thatcher, O. D.: Resistance to protamine zinc insulin without resistance to regular insulin in diabetes mellitus. *J. A. M. A.* 113:2411, 1939.
8. Beamer, C., and Eadie, G. S.: The role of epinephrine in the lack of response to insulin in diphtheria intoxication. *Am. J. Physiol.* 122:627-630, 1938.
9. Smith, F. H., and Smith, K. A.: The influence of muscular exercise on blood sugar concentrations. *J. Clin. Investigation* 16:283-301, 1937.
10. Harrop, G. A., Jr., and Benedict, E. M.: The participation of inorganic substances in carbohydrate metabolism. *J. Biol. Chem.* 59:683-697, 1924.
11. Kendall, E. C.: The influence of cortin, insulin and glucose on the metabolism of potassium. *Proc. Staff Meet., Mayo Clin.* 13:519-523, 1938.
12. Barnes, B. O.; Regan, J. F., and Nelson, W. O.: Improvement in experimental diabetes following administration of amniotin. *J. A. M. A.* 101:926, 1933.
13. Nelson, W. O., and Overholser, M. D.: The effect of oestrogenic hormone on experimental pancreatic diabetes in the monkey. *Endocrinology* 20:473-480, 1936.
14. Collip, J. B.: Inhibitory hormones and the principle of inverse response. *Ann. Int. Med.* 8:10-13, 1934.
15. Sjögren, B., and Svedberg, T.: The molecular weight of insulin. *J. Am. Chem. Soc.* 53:2657-2661, 1931.
16. Gordon, A. S.; Kleinberg, W., and Charipper, H. A.: Reticuloendothelial system and hormone refractoriness. *J. Exper. Med.* 70:333-345, 1939.

THE TREATMENT OF LEUKEMIA BY RADIO-ACTIVE PHOSPHORUS*

SHIELDS WARREN, MD †

BOSTON

IN THE course of a series of experiments on the effect of radiation from temporarily radio active phosphorus on cells and tissues, it became of interest to note this effect on some of the more sensitive human cells. The circulating leukocytes in human leukemia appeared to be the most suitable form to compare with the results obtained on certain animal tissues. Since a number of cases of leukemia had been treated with radio-active phosphorus from the Berkeley cyclotron by Lawrence and his associates,¹ this seemed to be a justifiable procedure. It has become well established, however, that satisfactory responses in chronic leukemias may be obtained, at least temporarily, by x ray irradiation. Consequently, it was held inadvisable to subject such patients to a new and relatively untried type of radiant energy, and cases of acute or subacute leukemia were selected, since in them the established methods of radiation therapy leave much to be desired.

The radio-active phosphorus used in the treatment of these cases was chiefly obtained from the Harvard cyclotron ‡. At first, red phosphorus bombarded in the target chamber of the cyclotron was utilized. Later, in order to obtain a more concentrated source, phosphorus in the form of iron phosphide was placed on a probe within the deuteron stream of the cyclotron. A portion of the phosphorus was thus made radio active. This phosphorus has a half-life of 14.5 days, and gives off a fairly penetrating beta radiation.

The phosphorus thus treated was changed by standard chemical methods to dibasic sodium phosphate. This was calibrated as to radio activity on a modified Lauritsen type electroscope. An error of approximately 10 per cent in measurement of very small samples exists. It is, however, amazingly sensitive, particles of radio active phosphorus as small as 3.5×10^{-14} mg. being detectable with its aid.

The desired amount of radio active phosphorus, ranging from 1 to 4 millicurie equivalents, was dissolved in 5 per cent glucose and physiologic saline

solution prepared for intravenous use, sterilized and injected intravenously into the patients. In all cases treated elsewhere the phosphorus had been given by mouth. Oral administration, however, has a disadvantage in that the proportion of phosphorus absorbed by way of the gastrointestinal tract is variable and frequently over 10 per cent may fail to be absorbed. On the basis of animal experiments,^{2,4} the injected phosphorus is shown to be absorbed selectively in the various organs and tissues. Fortunately, those in which the major deposit of leukemic cells occurs—the bones, the liver, the kidneys and the spleen—take up relatively large amounts.

In all the cases, the excretion of radio-active phosphorus was followed in the urine. That present in the feces, when the substance has been intravenously administered, is a relatively unimportant fraction. The concentration in the blood was checked from time to time in order that excessive doses should not be given. Large doses of radio active phosphorus have been shown to produce marked fibrosis and aplasia of the hematopoietic tissues.¹

The following are abstracts of the records of four cases of acute or subacute leukemia that have been treated.

CASE REPORTS

CASE 1. A 35-year-old man, referred by Dr. J. W. Norcross, of the Lahey Clinic, Boston, entered the Palmer Memorial Hospital on January 8, 1940, with a diagnosis of subacute myelogenous leukemia. The past history is particularly interesting in that the patient had been a professional blood donor for a number of years. Seven months previously he noticed weakness, and a diagnosis of myelogenous leukemia was made. He was given Fowler's solution and several transfusions. During several months x-ray treatment was given, without apparent general benefit, although the white-cell count was kept below 14,000 for some time. Numerous transfusions were given. He developed purpuric lesions of the skin. On admission the red-cell count was 3,500,000, with 0.5 per cent reticulocytes, the hemoglobin 62 per cent, the white-cell count 41,200 and the hematocrit reading 31 per cent. The differential count was 12 per cent polymorphonuclear leukocytes, 12 per cent band forms, with 95 per cent lymphocytes, 1 per cent eosinophils, 0.5 per cent abnormal monocytes, 4.5 per cent metamyelocytes, 60 per cent myelocytes, 4 per cent promyelocytes and 50.5 per cent blasts. The platelet count was 171,000.

On January 9 the patient received intravenously 750 cc. of 5 per cent glucose and physiologic saline containing 56 gm. of dibasic sodium phosphate, of which 2.6 millicurie equivalents of the phosphorus was radioactive. Frequent checks of the concentration of the blood and determina-

*From the New England Deaconess and Colls & P. Huntington Memorial hospitals.

†Aided by a research grant from Eli Lilly and Company Indianapolis, Ind.

‡Assistant professor of pathology, Harvard Medical School, pathologist at Colls & P. Huntington Memorial and New England Deaconess hospitals.

1. An indebted to Drs. K. T. Baubridge, R. Hickman and R. E. Curtiss for the preparation of the phosphorus. Two doses—used in Cases 2 and 3—were received from the Radlaton Laboratory at Berkeley, California through the courtesy of Drs. Ernest O. Lawrence and John H. Lawrence.

tions of the rate of excretion were made. There was no reaction following the injection except for a slight sensation of fullness and a dull ache in the lower back, which passed off in about 3 hours. The white-cell count after 2 days had dropped to 33,000. On the 3rd day the count rose to 75,300, with approximately the same differential as on admission. At the patient's request a 500 cc. transfusion was given, to which he had a severe reaction. He recovered promptly and felt very well.

On January 16 an additional dose of irradiated phosphorus was given intravenously—0.9 millicurie equivalent in 3.7 gm. of dibasic sodium phosphate dissolved in 500 cc. of 5 per cent glucose and physiologic saline solution. The following day the white-cell count was 27,300, and on January 19 it was 19,600. The differential count showed 6 per cent polymorphonuclears, 11.5 per cent band forms and 49 per cent blasts. On January 22 the white-cell count was 35,000, with a differential essentially similar to that given above.

The patient returned home, where he was considerably more active than he had been previously. The white-cell count on January 29 was 21,450. On January 31 and February 8 and 15 he received transfusions of 500 cc. On February 19 he was readmitted for further therapy; the white-cell count was 94,500 with 72 per cent blast forms. He showed several purpuric foci and a focus of swelling in the right calf. On February 20 he received intravenously 1.4 millicurie equivalents of radio active phosphorus in 700 cc. of 5 per cent glucose and physiologic saline. The next day the white-cell count dropped to 61,000, and 1 millicurie equivalent of radio-active phosphorus was given intravenously. The patient was discharged on February 21, with a white-cell count of 97,500, to spend the holiday at home. While he was there his breathing became obstructed, presumably by hemorrhage into the cervical muscles, and he died before aid could be obtained. Permission for an autopsy was not obtained.

CASE 2. A 55-year-old man, referred by Dr. Richard H. Sweet, of Boston, was admitted March 28, 1940, with a diagnosis of acute lymphatic leukemia. He was referred from the Chelsea Memorial Hospital, which he had entered March 8 with a history of a cold 1 week before entry, chills, pain in the left chest and the coughing of bloody sputum. There was a left-upper-lobe pneumonia, and a Type 32 pneumococcus was recovered from the sputum. On physical examination at that time the spleen and lymph nodes were enlarged and the white-cell count was over 100,000, the cells being chiefly lymphocytes. On entry to the Palmer Memorial Hospital, hematologic studies showed an acute lymphatic leukemia. The patient stated that he had noted some lumps in his neck. Previous to his present illness his appetite had been good; he had had no weakness or palpitation, and had worked at loading coal into a coke oven.

On admission the red-cell count was 4,300,000, the hemoglobin 76 per cent and the white-cell count 118,500, with 10 per cent polymorphonuclear leukocytes, 89 per cent lymphocytes and 1 per cent large mononuclears. On April 3 the white-cell count was 118,000. Examination of a biopsied lymph node from the left axilla showed acute lymphatic leukemia. X-ray therapy was given to the left lower lung field because of partial atelectasis of the left lower lobe, assumed to be due to mediastinal pressure.

On April 12 the white-cell count was 20,500, with 8 per cent polymorphonuclear leukocytes, 90 per cent lymphocytes and 2 per cent large mononuclears. That day the patient was given intravenously 3 millicurie equivalents of radio-active phosphorus in 7.3 gm. of dibasic sodium phosphate in 500 cc. of 5 per cent glucose and saline so-

lution. On April 25 the white-cell count was 7300, with 3 per cent polymorphonuclear leukocytes and 93 per cent lymphoid cells.

The patient's condition remained fairly satisfactory, with no complaint and no diminution in the swelling of the peripheral lymph nodes. On May 9 a bone-marrow biopsy was performed; the section showed a picture of acute

TABLE 1. *Study of Biopsied Bone-Marrow Specimens from Case 2.*

TYPE OF CELL	INCIDENCE	
	APRIL 8, 1940	MAY 9, 1940
	%	%
Hemohistioblasts	0.5	0.0
Hemocytoblasts	33.5	21.0
Myeloblasts	0.5	0.5
Premyelocytes	0.5	1.0
Myelocytes	1.5	4.0
Metamyelocytes	3.0	5.5
Polymorphonuclear leukocytes	1.5	5.0
Proerythroblasts	0.0	0.0
Basophilic erythroblasts	0.5	0.5
Polychromatic erythroblasts	1.0	8.0
Orthochromic erythroblasts	2.5	14.0
Monoblasts	0.0	0.0
Monocytes	0.0	0.0
Lymphoblasts	0.5	0.0
Prolymphocytes	2.5	0.0
Lymphocytes	52.0	40.5
Rieder-Türk plasma cells	0.0	0.0

lymphatic leukemia, with marked fragility of the lymphoblasts and small numbers of myeloid cells. A study of bone-marrow elements was made by Dr. Juan Picena. The results are shown and contrasted with earlier findings in Table 1.

On May 11 the patient received 2.8 millicurie equivalents of radio active phosphorus in 8 gm. of dibasic sodium phosphate. There was no reaction. He was discharged May 14 with a white-cell count of 7700; the polymorphonuclear leukocytes had increased to 52, and there were only 40 per cent lymphoid forms. The general condition continued good. On May 23 the weight was 132 pounds, a gain of 9 pounds since April 16.

On May 29 the patient was readmitted and 1.2 millicurie equivalent of radio-active phosphorus in 2.9 gm. of dibasic sodium phosphate in 500 cc. of 5 per cent glucose and saline solution was given intravenously, without reaction. The red-cell count was 3,010,000 and the white cell count 7500, with 44 per cent polymorphonuclear leukocytes. The patient was discharged on May 31.

On June 13 the patient appeared to be in satisfactory condition with no complaint, and there appeared to be slightly less swelling of the peripheral lymph nodes. On June 27 the condition was the same, and the white-cell count was 6400.

On August 6 the patient was readmitted for complete study. His condition was still good. The peripheral lymph nodes were approximately the same size as previously. The white-cell count was 6300, with 23 per cent polymorphonuclear leukocytes, in contrast with 118,500 and 10 per cent respectively on the first admission. It was intended to give him 2 millicurie equivalents of radio-active phosphorus, but owing to a reaction, with nausea and shortness of breath, the injection was discontinued after 0.6 millicurie equivalent had been given. The patient was discharged in satisfactory condition, and has continued active and without pain, although not strong enough to do heavy work.

On September 26 he received 15 millicurie equivalents of radio-active phosphorus intravenously, and was discharged with a white-cell count of 8450, of which 48 per cent were polymorphonuclear leukocytes. On October 17 he was moderately active, and his condition fair, with a red-cell count of 2,300,000 and a white-cell count of 8050 with 46 per cent polymorphonuclear leukocytes.

CASE 3 A 68 year-old man, referred by Dr. Howard F. Root, of Boston, was admitted April 11, 1940, with a diagnosis of acute lymphatic leukemia. For the previous few months he had been slightly short of breath and for 1 month had had some orthopnea. For 2 months he had noted swelling of the ankles in the daytime. On admission the red-cell count was 1,760,000, the hemoglobin 34 per cent and the white-cell count 42,550, with 19 per cent polymorphonuclear leukocytes, 75 per cent lymphoid cells, 4 per cent large mononuclears and 2 per cent eosinophils. The peripheral lymph nodes, liver and spleen were moderately enlarged.

On April 17 the patient received a transfusion of 500 cc of citrated blood. On April 18 he received intravenous 21 millicurie equivalents of radio-active phosphorus in

radio-active phosphorus in 1 gm of dibasic sodium phosphate in 800 cc of 5 per cent glucose and saline solution, without reaction. On July 15 he was given a 500-cc. transfusion, followed by febrile reaction. He was discharged temporarily improved July 16.

On September 25 he received 25 millicurie equivalents of radio-active phosphorus intravenously and was discharged with a white-cell count of 11,350, of which 57 per cent were polymorphonuclear leukocytes. On October 17 his condition was as before and he was working steadily, the red-cell count was 3,450,000, and the white cell count 9750 with 50 per cent polymorphonuclear leukocytes.

CASE 4 A 57 year-old man, referred by Dr. Richard L. V. Wingate, of Cambridge, was admitted June 26, 1940, with a diagnosis of subacute lymphatic leukemia. The red cell count was 3,450,000, the hemoglobin 65 per cent and the white cell count 126,500. All the white cells were of the lymphoid series. The platelets were decreased. In various portions of the body dull red, firm swellings had appeared, which ran a sluggish course, eventually drained necrotic material, and left a clean walled cavity which healed with the formation of a small scar. Practically all the lymph nodes were enlarged in varying degrees, the largest, in the right axilla, being 7 cm in diameter. The spleen was palpable 3 cm below the costal margin and the liver was palpable just below the costal margin.

On June 28 the patient received intravenously 4 millicurie equivalents of radio-active phosphorus in 0.8 gm of dibasic sodium phosphate in 500 cc of 5 per cent glucose in physiologic saline solution. There was no reaction. The general condition seemed fairly satisfactory. The white-cell count on the following day was 124,500, still with 100 per cent lymphoid cells. The patient was discharged June 30 and was readmitted July 9 having done fairly well since his last visit. The white-cell count was 77,750, the cells still being entirely of the lymphoid series. He had developed a brawny, red induration involving the lower ends of the right internal thigh muscles. This was somewhat painful and similar to the infiltration which he had earlier had elsewhere. On July 11 an aspiration biopsy of the sternum was done, which showed 18 per cent cells of the granulocytic series, 14 per cent of the erythrocytic, 28 per cent hemocytoblasts and the remainder lymphoid cells. The same day the patient received 1 millicurie equivalent of radio-active phosphorus, without reaction. Following this there was decided regression of the indurated region of the right thigh.

The patient was discharged July 12. He was to have returned to the Out Patient Department on August 8, but by that date he had had continued difficulty with the lesion in his right thigh. This had increased in size and had become markedly tender, finally discharging approximately 120 cc of thin, slightly hemorrhagic fluid. The remaining defect was clean, and closed in with apparently normal granulation tissue. On August 15 the general condition was less satisfactory, and death occurred in late September.

As has been pointed out by Lawrence,⁶ the doses of radio active phosphorus have been marked out empirically, and probably are not optimal. The intravenous method of administration, which we have used, seems most suitable. Careful study of the concentration of radio-active material in the blood and the rate of its excretion is important.

TABLE 2 Study of Biopsied Bone Marrow Specimens from Case 3

TYPE OF CELL	INCIDENCE		
	APRIL 22 1940	JUNE 6 1940	JULY 11 1940
Hemohistoblasts	0%	0%	0%
Hemocytoblasts	0.5	1.3	3.8
Myeloblasts	0.0	0.4	0.3
Premyelocytes	0.0	0.4	0.0
Myelocytes	0.5	0.8	0.6
Metamyelocytes	0.3	1.7	0.7
Polymorphonuclear leukocytes	0.9	3.3	1.4
Proerythroblasts	0.0	0.1	0.0
Basophilic erythroblasts	0.0	0.4	0.4
Polychromatic erythroblasts	0.5	1.3	1.1
Orthochromic erythroblasts	0.5	0.8	0.0
Lymphoblasts	3.3	2.5	4.0
Prolymphocytes	4.5	3.6	10.2
Lymphocytes	89.0	83.9	80.9
Reder Turk plasma cells	0.0	0.6	0.4
Monocytes	0.0	0.1	0.0

11 gm of dibasic sodium phosphate in 800 cc of 5 per cent glucose and saline solution. The following day the white cell count was 37,500. The results of sternal marrow biopsies April 22, June 6 and July 11 are shown in Table 2.

The patient was discharged improved April 23. He was active at home, and returned to the hospital May 8 on request. On May 11 the red cell count was 2,340,000, the hemoglobin 50 per cent and the white-cell count 19,850, with 27 per cent polymorphonuclear leukocytes and 59 per cent lymphoid forms. He then received intravenously 0.8 millicurie equivalent of radio active phosphorus in 550 cc of 5 per cent glucose and saline solution. He was discharged May 15 with a white-cell count of 17,200.

On June 3 the patient re-entered the hospital and received intravenously 3.9 millicurie equivalents in 155 gm of dibasic sodium phosphate in 500 cc of 5 per cent glucose, without reaction. On June 5 the white-cell count was 11,600. On June 6 the patient received a transfusion of 500 cc and was discharged.

On July 10 he re-entered, still feeling well. The red cell count was 2,570,000 and the white cell count 11,700, with 23 per cent polymorphonuclear leukocytes. The patient received intravenously 3.8 millicurie equivalents of

SUMMARY

Four cases of acute or subacute leukemia were treated with temporarily radio-active phosphorus prepared on the Harvard cyclotron and injected intravenously in the form of dibasic sodium phosphate. The doses ranged from 1 to 4 millicurie equivalents. Some improvement has been seen in two patients as evidenced by their general condition, level of white-cell count and condition of bone-marrow. These patients are moderately active. Two patients showed no significant response beyond minor changes in white-cell count; both are dead. This therapy is experimental, and does

not displace present methods of radiation for the treatment of leukemia.

195 Pilgrim Road

REFERENCES

1. Lawrence, J. H.; Scott, K. G., and Tuttle, L. W.: Studies on leukemia with aid of radioactive phosphorus. *Internat. Clin.* 3:33-58, 1939.
2. Hudson, J. C., and Cowing, R. F.: The use of Lauritsen electroscope under adverse weather conditions. *Rev. Scient. Instruments* 11:347, 1940.
3. Hevesy, G.; Hahn, L., and Rebbe, O.: Excretion of phosphorus. *D. Kgl. Danske Vidensk. Selskab. Biol. Meddelelser* 14:3-23, 1939.
4. Warren, S., and Cowing, R. F.: The distribution of doses of radioactive phosphorus in rodents. *J. Lab. & Clin. Med.* (in press).
5. Lawrence, J. H.: Nuclear physics and therapy: preliminary report on a new method for the treatment of leukemia and polycythemia. *Radiology* 35:51-60, 1940.

NOTES ON THE HISTORY OF RHEUMATISM AND GOUT*

ROBERT S. HORMELL, M.D.†

BOSTON

CHRONIC arthritis is probably the oldest disease of which we have definite evidence. Pemberton and Osgood¹ have collected examples of the disease from reports of fossils dating back in remote antiquity six hundred million years. The dinosaurs of a hundred million years ago can be imagined limping through the lush growth on their way to tumble into immortality in the ponds and slime. The earliest forebears of our cattle and horses, in the Eocene Period, the crocodile lying under an Egyptian sun fifteen million years ago and the camel of the Pliocene Era have left us their arthritic bones. The cave bear and the saber-toothed cat, of the Pleistocene Era, five hundred thousand years ago, died sufferers from spondylitis deformans. The Neolithic Man of seventy-five thousand years ago wielded his club with fingers as gnarled and stiffened as those we observe among our elders, while his weaker son had a "poker spine."

Egypt's sands have yielded remains of arthritic limbs. Smith and Jones² studied over ten thousand bodies from the Nile Valley, which ranged in time over a period of seven thousand years, from the prehistoric Nubians down through the Empire Period to the early Christian Copts. They found many cases of spondylitis deformans and even more cases of apparent osteoarthritis. None of these cases developed before the epiphyses had closed, and the authors do not report the finding of rheumatoid arthritis. They record only 1 case of true gout, and the patient was not a native Egyptian, but a Christian immigrant, prob-

ably from Syria.³ Sir Marc Armand Ruffer,⁴ however, has described lesions in Egyptian mummies compatible with those of rheumatoid arthritis as well as of osteoarthritis.

Hippocrates did not clearly differentiate the types of arthritic disease. In the *Prorrhetics*⁵ he remarks, "Of affections of the joints, the most dangerous are those seated in the thumb and great toe." And, he pronounces as incurable the occurrence of joint disease in persons "who are aged, have tofi in their joints, who have led a hard life and whose bowels are constipated," unless they have "an attack of dysentery, or other determination to the bowels."

In the *Aphorisms*,^{6,7} there are eighteen that refer to disease of the joints. He may have seen what is referred to today as menopausal arthritis, for he says: "A woman does not take the gout, unless her menses be stopped." The statement, "A young man does not take the gout until he indulges in coition,"⁷ might possibly have been a reference to the arthritis of a Neisserian infection. Hippocrates seems to have observed a connection between the sexual life and joint disease, as in the two aphorisms just quoted and also in his remark, "Eunuchs do not take the gout nor become bald."⁷

From this brief review it would seem that although Hippocrates saw many of the clinical types of arthritis, he made little attempt at classification. It is of general interest that he mentioned venesection, a practice which for centuries was the physician's first thought in therapy, and the origins of which seem lost in antiquity.⁸

The first century after Christ produced three im-

*Presented before the Boylston Medical Society, Boston, March 9, 1939.
†Intern, Fifth (Harvard) Surgical Service, Boston City Hospital.

important and accessible writers, Celsus and Galen at Rome, and Aretaeus in Byzantium. Celsus⁹ draws largely from Hippocrates, as when he remarks: "Joint disorders, too, such as foot and hand aches, if they attack young people and have not induced callosities, can be resolved; for the most part they are removed by dysenteries and fluid motions, whatever the sort."¹⁰ He also relates Hippocratic remarks on the menopause and in coition,^{7, 11} on the occurrence of pain in spring and fall^{6, 12} and on the subsidence of pain within forty days.^{6, 13} Celsus does not attempt to classify the arthritides. He discussed rheumatic fever unknowingly when he wrote: "Children in whom there has been nose-bleeding, which then has ceased, are sure to be troubled by pains in the head, or they get some severe joint ulcerations, or they also become debilitated by disease."¹⁴

Galen applied the theory of humoral pathology to arthritis, and seems to have distinguished gout as a separate entity, a new form of podagra that was hereditary and related to luxurious eating and drinking.¹⁵

Aretaeus gives a good account of the clinical picture of what resembles rheumatoid arthritis, describing the onset in small joints, the spread through the body, systemic changes and deformities. He, also, must have referred to rheumatic fever when he wrote, "In many cases, the gout has passed into dropsy and sometimes into asthma, and from this succession there is no escape."¹⁶

In the Byzantine Empire during the sixth and seventh centuries lived two of the later Greek compilers, Alexander of Tralles and Paul of Aegina. They drew from both Greece and Rome. Their writings summarize the system of medicine which developed from the Greek theory of humoral pathology.*

Alexander of Tralles lists the following causes of "podagre": effusions of hot blood into the joint cavity, defluxions of bile, of black bile, of phlegm, and alterations of the simple quality of the humors.¹⁸ His clinical types do not correspond to our clinical entities, but they served him as the basis for an extensive therapeutic scheme.

Paul of Aegina considered the disease to be due to "a preternatural humor and a weakness of the parts meeting together. . . . The prevailing humor is sometimes bilious, sometimes sanguineous, sometimes melancholic, but for the most part it is pituitous and crude, being engendered by excess of

food, indigestion and want of exercise."¹⁹ He gives a complete list of "precursory causes" that includes a good deal that is applicable today. Even now little can be added to what he said about etiology: "And some from accidents, as a blow, a sprain or the like, experienced the first attack of this complaint, the materials of the disease having previously lain quiet in the system until roused by the proximate cause."¹⁹ "Sorrow, care and other passions of the mind" are on his list.

The joint of bilious humor, according to Paul,²⁰ was pale, red, hot and acutely painful without much swelling. That of the melancholic humor was characterized by a dark skin. That of the pituitous humor had a white and watery skin, with the pain and swelling lying latent and developing slowly. The joint in the grip of the sanguineous humor had a sanguineous color.

The Arabian, Avicenna, 980-1036, was a famous and skilled physician, whose *Canon of Medicine*²¹ was a leading medical text. He mentions "gout" attacks, pain in the joints, sciatica, pain in the back and hips, and in Book III, as yet untranslated, he devotes a section to the special pathology of muscles, joints and feet.

The term "gout" is derived from the Latin *gutta*. Alexander of Tralles²² is said to have used it in the sixth century in the sense of arthritic disease. Radulfe²³ in the thirteenth century again used the word. Ballonius (Guillaume de Bailou),²⁴ a graduate of the University of Paris in 1570, first used the word "rheumatism" as a name for acute arthritis. *Gutta* in its original meaning stood for droppings from the nose. "Rheum" likewise means a watery or catarrhal discharge, and is derived from the Greek *ῥέω*, "to flow." Both terms are derived from words with the same fundamental meaning; their application to arthritis came about through the humoral theory of this disease.

From the seventeenth century onward come the descriptions of specific arthritic conditions. Richard Wiseman,²⁵ King Charles II's surgeon general, in 1672 described a specific entity, "tumor albus," that we now recognize as tuberculosis of the joints.

Thomas Sydenham,²⁶ 1624-1689, is responsible for clearly separating gout from acute and chronic arthritis. He²⁷ wrote a vivid account of the gout, the more vivid since he himself was a sufferer from the disease and died from the effects of nephrolithiasis. He wrote, in *Of a Rheumatism*;

When this Disease is not accompany'd with a Fever, it is often taken for the Gout, tho it differs essentially from that, as plainly appears to any one that well con-

*Plato and Aristotle taught that there were four qualities—hot, cold, moist and dry—and four bodily humors—blood, bile, black bile and phlegm. Health was the equisite of the humors, disease the imbalance. They were classified in systems according to the qualities they contained. The theory was based on the Hippocratic teaching that "diseases are cured by their contraries."¹⁷

siders both diseases. . . It is frequent enough now, and though it seldom kills anyone when the Fever is off, yet upon the account of the Violence of the Pain, and the Continuance of it, it is not contemptible.²⁸

Sydenham also clearly distinguished between the acute and chronic forms of arthritis. He spoke of the chronicity of arthritis, of remissions and exacerbations, of flexion deformities and ankylosis. He introduced the term "scorbutical rheumatism," but it is not clear whether this is intended to cover cases of arthritis associated with clinical scurvy, or is a catchall to hold cases that had the features of both gout and chronic rheumatism.²⁹

Boerhaave,³⁰ who lived in Leyden in the early eighteenth century, taught that there were two diseases, gout and rheumatism. The latter probably included without differentiation all our modern types of arthritis deformans.

Cullen's *Methodical System of Nosology*,³¹ divides all disease into fevers, neuroses, cachexias and local disorders. Among the fevers Cullen lists the arthritic diseases in the following groups: rheumatism, arthrodynia ("the consequence of the rheumatism"), odontalgia, podagra (gout) and arthropoiosis.³¹

Heberden,³² in 1782, described the arthritic nodes which go by his name, but his successor, Haygarth, first associated these nodes with a disease entity. To quote from his *Clinical History of the Nodosities of the Joints*:

There is one painful and troublesome disease of the joints of a peculiar nature, and clearly distinguished from all others by symptoms manifestly different from the Gout, and from Acute and Chronick Rheumatism.³³ . . . This disease has hitherto passed under the name of Gout or Rheumatism, or perhaps has been most commonly called Rheumatick Gout. . . I have ventured to call it the Nodosity of the Joints.³⁴

Haygarth also described, in 170 of the 10,459 patients on whom he kept careful clinical records, a disease called "acute rheumatism or rheumatic fever." He lacked by two decades the advantages of the stethoscope and therefore did not recognize heart disease in his patient who died: "On the tenth Day . . . the swelling of the Hands receded; her breath became shorter, with cough and spitting of blood which soon terminated fatally. . . . The Rheumatick inflammation seems here to have been translated from the joints to the lungs."³⁵

Scudamore's classic *Treatise on the Nature and Cure of Rheumatism* first appeared in 1817. It is noteworthy for an excellent survey of ancient and contemporary literature, and for its proposition that rheumatism was "pain of a peculiar kind,

usually attended with inflammatory action, affecting the white fibrous textures belonging to muscles and joints. . . ."³⁶ His classification included gout and rheumatism — acute, subacute and chronic.

During Scudamore's lifetime came the realization that heart disease was regularly associated with rheumatic fever. The 1827 edition of his treatise contains an extensive review of the early literature on this subject. He wrote, "There is not, probably, a more dangerous form of disease, than a sudden seizure of the heart during the inflammatory state of the system in acute rheumatism."³⁷ According to Scudamore, Dr. David Pitcairn, at St. Bartholomew's Hospital, taught as early as 1788 that "persons subject to rheumatism, were attacked more frequently than others, with symptoms of an organic disease of the heart . . . and . . . called the latter disease 'Rheumatism of the Heart.'<"³⁸ This statement is said to have first appeared "in the second edition of Dr. Baillie's *Morbid Anatomy*, which was published in 1797,"³⁹ and was taken by Scudamore from a paper by Dr. J. C. Wells, "On Rheumatism of the Heart,"⁴⁰ in the *Edinburgh Medical Journal* for 1806 a review of Dr. Odier's *Manuel de médecine pratique* stated that Odier wrote of rheumatic affection of the heart.³⁹ A paper by Sir David Dundas, in the first volume of *Medical and Chirurgical Transactions*, described 9 cases of rheumatic disease of the heart, of which 6 were examined post mortem.* Thus by 1812 rheumatic heart disease was definitely known.

However, in these accounts there are no descriptions of valvular disease or of endocardial involvement; they describe the symptoms of palpitation, breathlessness and anasarca, and the pathology of cardiac enlargement and pericarditis. It was not until after the invention of the stethoscope in 1819 that the valvular involvement could be described during life.

Thus Bouillaud is generally credited with the first description of rheumatic heart disease. In 1832-1833 he described cases of endocarditis and pericarditis associated with acute rheumatism. His famous Law of Coincidence established the occurrence of heart disease both concomitantly with and as a sequel to acute articular rheumatism.⁴² He noticed and described cardiac enlargement, change in the shape of the chest, "a bellows, file or saw sound," irregularities in the pulse and "different abnormal sounds, some arising from the rubbing of the opposite coats of the pericardium against each other, others from the

*These cases are discussed at length in a footnote in Scudamore and Dundas's conclusion, Scudamore then (1817) stated, "I should rather be disposed to consider the general rheumatism of the constitution to be a predisposing cause of this disease of the heart rather than to pronounce it rheumatism of this organ."

complication of pericarditis with valvular endocarditis."⁴³ However, he was far from the truth when he wrote:

People long ago talked vaguely of gout flying to the heart, of rheumatism translated to the heart, &c. &c. But as the nature of these gouty and rheumatic metastases had never been determined, they were considered to be accidents and not very common occurrences. A little later, in speaking of rheumatic metastases, observers placed, it is true, pericarditis among the number of accidents which these metastases were capable of producing, but they spoke of it slightly or incidentally.⁴⁴

It is but a relatively short time from 1833 to the present. The recent history of the problem of classification of arthritic disease is complicated, but has been well covered by several authors.^{1, 23, 46}

I propose to return to the ancient world to review old methods of therapy. Hippocrates' methods of therapy are quite conservative. He mentions diet, regimen, baths, warm climate, purging and local applications. He does not lay down a schedule of rules for the treatment of arthritis.

Celsus is rich in methods of treatment. He¹¹ advised hot fomentations to the joints, hot plasters or cataplasms, and emollients as external applications. He recommended cupping and burning the skin with cauteries "to set up issues." These ulcers were to be kept open and massage was to be used, "in order that the materials of the disease, which have been doing harm by collecting, may be the more readily dispersed." He mentions bloodletting and the use of diuretics and clysters. He shows the Hippocratic influence in advising the patient to refrain "from wine, mead and venery for a whole year," and to use a regime of mild exercise, sweating, local application of oil, diuretics, purging and a diet "of the middle class."¹²

For severe pain Celsus recommends an ointment made of rind of poppy heads, boiled in oil and mixed with wax salve made of rose oil. One form of treatment that he mentions is of extraordinary interest. "The stone, too (which corrodes flesh), which the Greeks call sarcophagos, is carved out so as to admit the feet; when these are painful, they are inserted and held there, and are usually relieved."¹³ No other reference to immobilization was found until some thirty years ago, when orthopedic surgeons began to use plaster-of-Paris casts for the immobilization of arthritic joints.

It is in Aretaeus that we first find reference to internal medication for which claims to specificity are made. Thus he wrote: "In gouty cases hellebore is the great remedy."⁴⁶ Hellebore contains veratrine, the only modern use of which is as a

cardiac depressant, but its action in Greek medicine was probably as a desired purgative and for diuretic action. Aretaeus includes a significantly long list of common herbs useful for cataplasms, among which are "bread with the cooling parts of gourd and pompion, and simple cucumber, and the herb plantain and rose leaves."⁴⁶ Other common plants used by him are root of comfrey, herb cinquefoil, horehound with narrow leaves, parts of the citrous fruit not good to eat, dried figs and barley meal. We can see the pharmacopeia in its evolutionary process in such lists as these. One method of treatment he advised is "Let a goat feed on the herb iris, and when it is filled therewith, having waited until the food it has taken be digested in the stomach, let the goat be slaughtered, and bury the feet in faeces within the belly."⁴⁶

Aretaeus has faith in his ability to cure early cases, but not well-established ones. He describes the usual course of a case of arthritis:

Pain seizes the great toe; then the forepart of the heel on which we lean; next it comes into the hollow of the foot, but the ankle swells last; and they blame a wrong cause; some, the friction of a new shoe; others, a long walk; another again, a stroke or being trod upon; . . . On this account the disease gets to an incurable state, because at the commencement, when it is feeble, the physician is not at hand to contend with it; but if it has acquired strength from time, all treatment is useless.⁴⁷

Alexander of Tralles⁴⁸ mentions the drug hermodactylus, or colchicum. He states that this will at once relieve arthritic pain, if given internally with pepper, anise, ginger, aloes and scammony. Colchicum has a remarkable history. Paul of Aegina in the seventh century states:

Some, in the paroxysms of all arthritic diseases, have recourse to purging with hermodactylus; but it is to be remarked that hermodactylus is bad for the stomach, producing nausea and anorexia, and ought, therefore, to be used only in the case of those who are pressed by urgent business; for it removes rheumatism speedily, and after two days at most, so that they are enabled to resume their accustomed employment.⁴⁹

According to Francis Adams,⁵⁰ Avicenna and Rhazes used colchicum, and Lanfrancus, "an early modern writer," mentioned it. However, because of its toxicity, somewhere the drug was condemned, and it was not used by Sydenham. It was rediscovered by Stoerck in Vienna in 1763, and soon took its proper place in medicine.⁵¹

Alexander had a different regime for each of his four types of arthritic complaint, based on the humoral qualities he believed to cause the disease.⁵² For the bilious type there was a careful diet containing nothing bile-forming, a regime of moderate exercise, baths and an elaborate list of local

applications. The phlegmatic joint was injured by refrigerants, helped by calefacients; he approved blistering with cantharides, but not burning with iscae, which were local applications of flax and oil, set afire over the joint.⁵³ This practice of burning flax was mentioned in Hippocrates⁵⁴ and had its counterpart in Chinese and Indian medicine, where the burned substance was a moss, *moxa*.⁵⁵ Moxae were reintroduced during the seventeenth century; we find in Sydenham's writings a criticism of their use.⁵⁶ For the sanguineous type, bloodletting was indicated, including evacuation of blood from the joint space,⁵⁷ and articles of diet engendering blood were proscribed. Alexander's blood-builders were flesh, pork and sweet wine. For tophi, he recommended litharge, old oil, Dragon's blood, niter, turpentine and ammonia as local applications.⁵⁸

Paul of Aegina had very similar methods. For the bilious humor he used purgative medicines "such as that from rhodomel, that from quinces, the antidote called picra and aloetic pills."⁵⁹ While the pain was acute he advised local applications, paregoric substances and narcotics. He recommended hermodactylus, purging and bloodletting for the sanguineous variety.⁴⁹ For the pituitous type he had what is practically a list of garden herbs—cabbage, parsley, vervain and fleabane—as local applications. A cataplasm of ox or goat's dung, honey, boiled barley meal, in oxycrate, was among his more picturesque remedies.⁴⁹

For tophi, Paul advises the use of these mixtures:

This is an excellent application for tophi in the joints: very old and acrid cheese pounded and applied with a decoction of fat swines' flesh, it also being old. . . .⁶⁰ The composition from dragon's blood is of wonderful efficacy for chalkstones and many other complaints, but is difficult to procure.⁶⁰

The ancient equivalent of our steam bath is described thus:

Some, for the entire removal of the complaint, boil whole wolves in oil, wherewith they cure arthritic cases; . . . And in like manner they boil hyaenas, making a discutient oil from them; and then filling the cistern of the bath with it, and putting the arthritic patients into it. . . .⁶⁰

Avicenna, four centuries later, recommended baths of hot oil, more beneficial "if the flesh of the jackal or hyaena is boiled in it."²¹ He also advised evacuant measures against the gout.²¹ He used desiccants on the skin for a swollen joint, "as one does in the case of those afflicted with dropsy."²¹

The familiar propensity of the Arabians to use psychotherapy is illustrated by two tales from an Arabic collection of stories of the great physicians, called *Four Discourses*, which dates from about

1155 A.D. and is from the pen of the court physician of Samarkand.⁶¹ In the first, Rhazes was called to attend the great lord, Amir Mansur, in Transoxiana, who suffered from rheumatism. After exhausting all his skill, Rhazes said to him, "Tomorrow I will try a new treatment, but it will cost you the best horse and mule in your stables." The next day Rhazes gave the amir douches of hot water and a draught which he had prepared, until the humors of his joints were matured. Then Rhazes took a knife into his hand, and stood for a while reviling the amir, telling him he was about to destroy him. The amir was furious, and partly from rage and partly from fear sprang to his feet. Rhazes immediately fled the country on the steeds that the amir had given him. Once safe across the Oxus, Rhazes wrote to the amir, explaining how his psychotherapeusis had worked to increase the natural caloric, which thus gained sufficient strength to dissolve the already softened humors. He closed by saying that it was inexpedient that they should meet again.

The second story is told of an unnamed court physician who was taken to treat a woman of the King's household for stiffness of the joints. He had recourse to psychic treatment: by first removing the woman's veil and then her skirt he called to his aid the emotion of shame, whereby a flush of heat was produced within her which dissolved the rheumatic humor.

From the Arabians it was five hundred years to Sydenham,²⁷ but in essentials the therapy of arthritis had not changed. Yet in one important respect Sydenham was far ahead of his time. He conceived of arthritic disease and gout as chronic diseases, and recommended a conservative regime. The patient should go to bed early and rise early, should keep the mind easy, should exercise regularly and should abstain from coition. He should refuse wine, and should substitute for it a "Dietetick Drink." This was a concoction of sarsaparilla, sassafras wood, china root, licorice root, anise seed and water. Of this he said, "Tho' the constant taking of them may cause some loathing for a week or two, they will afterward be as pleasing, and as acceptable, as any other liquors, to which he has been most accustomed."

Sydenham has a great deal to say against wine:

For tho' it may supposed to do Good, by helping the Concoctions, the Disorders whereof I have long accounted the antecedent Cause of the Gout; yet, with respect to the containing Cause, it must be reckoned wholly injurious, for that it fires and exagitates the Humors, the Fomes of the disease, already prepared to give Battle. . . . Therefore those that are subject to the Gout, must take care that they use those Liquors that can neither cause Drunkenness when they are

taken in a large Quantity, nor injure the Stomach, by chilling it. . . . I count Water, by itself, crude and injurious; and I have found it so to my Hurt. but Water may be safely drunk by young People.

For the treatment of the acute attack he recommended laudanum, mild purging and sweating. He does not mention colchicum, and conservatively he disapproves of much bloodletting.

Sydenham's treatment of acute arthritis was quite different.⁶² This included the customary bleeding, a sweet tasting julep "to be drunk at leisure," local applications of cold to the joints and "glisters" of sugar and milk or sugar and violet water. He insisted that the patient be out of bed for part of the day, "for keeping bed constantly promotes and augments the Disease."⁶³

He made use of electuaries, and in his treatise printed the formulas of two, a stomachic and an antiscorbutic. The latter included the "peels of six oranges" but no other citrous fruit.⁶⁴ The digestive electuary was a compound of the dried powders of thirty herbs, "gathered when they have most Virtue in them," dried in paper bags, and mixed with purified honey and canary wine.⁶⁵

In the year 1805, when Haygarth wrote his *Clinical History*, his treatment of gout and arthritis had a modern tone. The following remedies were found useful: guaiacum, cinchona, leeches, "Warm Bathing and Pumping at Bath . . . at Buxton," vapor baths, sea baths, antimony, meze-reum,* aconite, and the external use of oil and camphor and "bootikins."⁶⁶ For rheumatic fever he used bleeding, antimony, sudorifics, saline medicines, warm baths and Peruvian bark.⁶⁵

In the work of Bouillaud we have seen the stethoscope in action. It is strange that this man, who was so modern in his method of investigation, should be the worst bloodletter of whom we read. For the treatment of acute rheumatic fever he recommended bleeding four or five bowls the first day, then three bowls each the second and third days, followed by later bleeding by leeching, and venesection if the patient relapsed. He claimed to have treated 184 cases of acute rheumatic fever by this method, and said, "All of them have been cured except one."⁶⁶ He complained:

Truly we know not why so many daily say that they bleed the same as we do, and that nevertheless they do not obtain the results which we announce. No, emphatically no; they do not bleed according to our method, whatever may be said to the contrary.⁶⁷

Bouillaud wrote these words in 1832. The stethoscope had been introduced, and had recently been given by vote the approval of the Boylston Medical Society of Harvard Medical School as an instrument likely to become useful in the clinic. Virchow was then a schoolboy who was to study fossils in the caves of the Pyrenees and introduce the term "arthritis deformans." The work of Charcot in France, of Robert Adams and Garrod in England, and of Goldthwait, Nichols and Richardson and others of their notable group in Boston, and Pemberton in Philadelphia, plunged the notions of arthritic classification into a welter of confusion, but eventually clarified and simplified the picture and led to the present workable classification. Medieval methods of bleeding, purging, puking and cupping were to give way before a therapy based on clinical and laboratory investigation of etiologic factors. The investigation is still going on, and our knowledge of specific causes is still incomplete. The nature, etiology and specific therapy of arthritis deformans remain among our most alluring medical problems, pre-eminent in medical, social and economic importance.

REFERENCES

- 1 Pemberton R, and Osgood R B *The Medical and Orthopaedic Management of Chronic Arthritis* 403 pp New York Macmillan Co, 1934 P 17
- 2 Smith C E and Jones P W *Archaeological Survey of Nubia Report for 1907-1908* Vol II *Archaeology on the Human Remains* 378 pp Cairo National Printing Department, 1910 P 270-278
- 3 Smith and Jones p 269
- 4 Ruffer, M A *Studies in the Paleopathology of Egypt* 372 pp. Chicago University of Chicago Press 1921 P 212-267
- 5 Hippocrates *The Genuine Works of Hippocrates* Translated from the Greek, with a preliminary discourse and annotations by Francis Adams Vol I 390 pp New York William Wood & Co, 1856 P 217
- 6 *Idem The Genuine Works of Hippocrates* Vol II 366 pp New York William Wood & Co, 1886 P 215, 218, 224, 227, 232, 239, 244 258 260 and 270
- 7 Hippocrates⁸ pp 254 255
- 8 Hippocrates⁹ p 179
- 9 Celsus A C *De medicina* Translated by W G Spencer, Vol I 499 pp Vol II and III 722 pp Cambridge, Massachusetts Harvard University Press 1935 and 1938
- 10 Celsus⁹ Vol I p 137
- 11 Celsus¹⁰ p 455
- 12 Celsus¹⁰ p 457
- 13 Celsus¹⁰ p 459
- 14 Celsus¹⁰ p 119
- 15 Galen cited by Spencer in Celsus¹⁰ p 464 Also cited by Adams¹⁰ p 667
- 16 Aretaeus *The Extant Works of Aretaeus, the Cappadocian* Translated by Francis Adams 510 pp London Sydenham Society, 1856 P 32-35
- 17 Garrison, F H *An Introduction to the History of Medicine With medical chronology, suggestions for study and bibliographic data* Second edition 905 pp Philadelphia and London W. B Saunders Co, 1917 P 77 Hippocrates¹⁰ p 204
- 18 Alexander *Oeuvres médicales d'Alexandre de Tralles* Translated into French by F Brunet Vol IV 292 pp Paris Paul Geuthner, 1937. P 193
- 19 Paulus Aegineta *The Seven Books of Paulus Aegineta* Translated from the Greek by Francis Adams Vol I 633 pp London Sydenham Society 1844 P 657.
- 20 Paulus Aegineta¹⁰ p 658
- 21 Greuter G C *A Treatise on the Canon of Medicine of Avicenna Incorporating a translation of the first book* 612 pp London Luzac & Co, 1930 P 191, 239, 435 and 479
- 22 Alexander cited in Celsus¹⁰ p 463
- 23 Radcliffe cited by Pemberton and Osgood¹ p 5 Also by Poynton, P J *Rheumatism In A Short History of Some Common Diseases* Edited by W Reit 211 pp London Oxford University Press, 1934 P 60
- 24 Bouillaud G: *Medici Parisiens Celeberrimi, Consiliorum Medicinalium* Vol III 331 pp Paris Jacobum Oueinell, 1643 P 17
- 25 Wieman R *Eight Chirurgical Treatises* Fifth edition Vol. I 504 pp London B Tooke et al. 1719 P 4/6

*The dried bark of *Daphne mezereum*, containing a glucoside daphnin

†The Peruvian bark had been brought to Europe from South America in 1620 by the Spanish. Its quinine was to prove a great addition to the physician's armamentarium. Sydenham in 1670 already had recommended it as the best sample for arthritis. Haygarth later his clinical results with Peruvian bark complete with case summaries in the most approved modern manner

26. Sydenham, T.: *The Whole Works of That Excellent Practical Physician, Dr. Thomas Sydenham*. Translated by John Pechey. Tenth edition. 447 pp. London: W. Feales, 1734.
27. Sydenham²⁰: pp. 341-354.
28. Sydenham²⁰: p. 200.
29. Sydenham²¹: p. 204.
30. Boerhaave, H.: *Boerhaave's Aphorisms: Concerning the knowledge and cure of diseases*. Translated from the last edition printed in Latin at Leyden, 1728, by J. Delacoste. 444 pp. London: W. Innys, 1742. Pp. 372, 383-385.
31. Cullen, W.: *A Methodical System of Nosology*. Translated by Eldad Lewis. 231 pp. Stockbridge: Cornelius Sturtevant, 1807.
32. Heberden, W.: *Commentaries on the History and Cure of Diseases*. Second edition. 518 pp. London: T. Payne, 1803. P. 148.
33. Haygarth, J.: *A Clinical History of the Acute Rheumatism, or Rheumatick Fever and A Clinical History of the Nodosity of the Joints*. 202 pp. London: Cadell and Davies, 1813. P. 181.
34. Haygarth²²: p. 188.
35. Haygarth²³: p. 83.
36. Scudamore, C.: *A Treatise on the Nature and Cure of Rheumatism: With observations on rheumatic neuralgia, and on spasmodic neuralgia or tic douloureux*. 589 pp. London: Longman, Rees, Orme, Brown & Green, 1827. P. 11.
37. Scudamore²⁴: p. 122.
38. Scudamore²⁵: p. 126.
39. Scudamore²⁶: p. 127.
40. Wells, J. C.: cited by Scudamore²⁶: p. 126.
41. Scudamore, C.: *A Treatise on the Nature and Cure of Gout and Rheumatism*. Second edition. 592 pp. London: Longman, Hurst, Rees, Orme and Brown, 1817. P. 523.
42. Bouillaud, J. B.: *New Researches on Acute Articular Rheumatism*. Translated by James Kitchen. 64 pp. Philadelphia: Haswell, Barington, and Haswell, 1837. P. 12.
43. Bouillaud⁴²: p. 15.
44. Bouillaud⁴²: p. 10.
45. Messeloff, C. R.: Historical aspects of rheumatism. *Med. Life* 37:3-5, 1930.
46. Aretaeus¹⁶: p. 493.
47. Aretaeus¹⁶: p. 363.
48. Alexander¹⁸: p. 246.
49. Paulus Aegineta¹⁹: p. 660.
50. Paulus Aegineta¹⁹: p. 675.
51. Sollman, T.: *A Manual of Pharmacology and Its Applications to Therapeutics and Toxicology*. Fifth edition. 1190 pp. Philadelphia and London: W. B. Saunders Co., 1936. P. 542.
52. Alexander¹⁸: p. 197.
53. Alexander: cited by Paulus Aegineta¹⁹: p. 669.
54. Hippocrates: cited by Sydenham, T.: *The Entire Works of Dr. Thomas Sydenham*. Translated by John Swan. 623 pp. London: Edward Cave, 1742. P. 460.
55. Garrison¹⁷: pp. 22, 62, 64, 283.
56. Sydenham²⁴: p. 461.
57. Alexander¹⁸: p. 234.
58. Alexander¹⁸: pp. 238-265.
59. Paulus Aegineta¹⁹: p. 658.
60. Paulus Aegineta¹⁹: p. 665.
61. Browne, E. G.: *Arabian Medicine*. 138 pp. Cambridge: University Press, 1921. Pp. 82-84.
62. Sydenham²⁰: pp. 202-204.
63. Sydenham²⁰: p. 205.
64. Haygarth²³: p. 193.
65. Haygarth²³: pp. 56-59.
66. Bouillaud⁴²: p. 59.
67. Bouillaud⁴²: p. 58.

CARCINOMA OF THE BREAST IN A TEN-YEAR-OLD GIRL*

Report of a Case

JOHN B. SEARS, M.D.,† AND MONROE J. SCHLESINGER, M.D.‡

BOSTON

IN THE last three decades only two well-authenticated cases of breast cancer before puberty have been reported,^{1,2} one in a girl of eleven, the other in a girl of twelve.

Deaver and McFarland³ quote Thompson's authenticated case (1908) of adenocarcinoma of the left breast in an eleven-year-old girl. Although its existence had been known for a period of three years, the growth had not increased in size until shortly before admission to the hospital.

The occurrence of carcinoma of the breast in the decade following puberty is extremely, though less, rare. Lee,⁴ in his study of 303 cases of breast cancer, found that the 2 youngest cases were both women of twenty-two. Hall and Bagby,⁵ in reviewing 134 patients under the age of thirty-one with all types of carcinoma, found 22 proved cases of breast cancer; of these the 2 youngest were twenty-two. Krauss and Kline,⁶ in their review of the literature in 1926, found 12 cases of confirmed unilateral carcinoma of the breast in patients under twenty-two.

CASE REPORT

A 10-year-old white, American-Irish schoolgirl (No. 44685) entered the Out-Patient Department of the Beth

*From the Department of Surgery and the Department of Pathology, Beth Israel Hospital and Harvard Medical School.

†Assistant in surgery, Harvard Medical School; outpatient surgeon to Vascular Clinic, Beth Israel Hospital.

‡Associate in pathology, Harvard Medical School; director of pathology, Beth Israel Hospital.

Israel Hospital on December 14, 1938, because of a lump in the right breast. Six years previously her mother had noted the lump. The child said she had hit her right chest on a car door that day. The mother believed that it might have grown during the previous year. There was no history of pain or tenderness. The patient had had measles, whooping cough and mumps before the age of 5. She was a normal, happy child. The mother was well. The father had died of pneumonia at 41.

Physical examination revealed a nodule 3 by 2½ by 2½ cm. under the right nipple. It was hard, irregular, sharply circumscribed, nontender and adherent to the overlying nipple, which was flattened. The mass was freely movable posteriorly. There were no lymph nodes in the axilla or supraclavicular region. X-ray examination of the tumor showed no evidence of calcification; that of the long bones, skull and chest showed no evidence of metastasis. The urinalysis was not remarkable. The red-cell count was 4,180,000, the hemoglobin 77 per cent (Sahli) and the white-cell count 10,000. The differential count was not unusual. Blood Hinton and Kahn tests were negative.

On December 16 the breast tumor and pectoral fascia were excised. A curved incision was made along the lower aspect of the tumor, which was exposed and found to be resting on the pectoral fascia. It had clear-cut borders on all surfaces except in its relation to the skin, to which it was firmly adherent. The tumor itself was firm and smooth. It was dissected from the overlying skin with difficulty and submitted for immediate frozen section. When the pathologist reported the presence of carcinoma, a wide skin area was excised, also the fascia overlying the pectoralis major. The border of the pectoralis was explored, and no lymph nodes were felt. One finger was introduced into the axilla, where no nodes were palpated. The wound was closed without drainage. The patient was discharged 8 days after the operation to the Tumor

Clinic for follow-up. At the end of a year there was no evidence of recurrence.

The pathologist's report was as follows:

The specimen consists of a globular mass 2 cm. in diameter. The external surface is pink-gray, smooth and dull. Attached to it are several small lobules of pink-yellow fat. The consistence is uniformly somewhat firm. On cross-section the specimen cuts with a gritty sensation. Most of the cut surface is glistening and gray, with one small irregular, tan-yellow area. The point of a dull instrument applied to the cut surface causes no pitting. On squeezing and scraping the cut surface, a small amount of fluid is obtained. Immediate frozen section reveals carcinoma.

Microscopic section shows the tumor to be fairly well-demarcated from the surrounding thin rim of breast tissue. In most areas there is an encapsulating layer of concentrically laminated fibrous tissue about the



FIGURE 1.

tumor. This layer is contiguous with the fibrous-tissue septums of the breast. In no place is the encapsulating layer very thick; in many places it is extremely thin, and in a few spots the enclosed neoplastic epithelial cells are invading the thin encapsulating fibrous tissue (Fig. 1).

There is considerable variation throughout the tumor in the proportion of fibrous tissue stroma to carcinomatous tissue. In only a few fields is there much fibrous tissue, whereas many fields consist almost entirely of epithelial cells. There is no necrosis or inflammatory reaction within the neoplasm itself, but there are a few lymphocytes in the tissues about the tumor.

The neoplastic epithelial cells are arranged in large sheets and cords and also in small irregular masses

(Fig. 2). There is no constant configuration. The individual cells in general have poorly defined walls and a moderate amount of cytoplasm. The nuclei are round to slightly oval, slightly hypochromatic and quite uniform in size; many have a prominent nucleolus. Mitotic figures are few in number. Within some of the masses of epithelial cells there is a hint of acinar formation. In these areas the cells tend to surround a small lumen, which is either empty or contains a small globule of hyaline-appearing material. In other places a short stretch of high columnar cells is



FIGURE 2.

arranged along a collagenous streak. In many places, including several spots along the capsular surface, the neoplastic cells infiltrate the collagenous stroma.

Diagnosis: adenocarcinoma of breast, Grade II.

The diagnosis of carcinoma was confirmed by Drs. Shields Warren, Charles F. Geschickter, Tracy B. Mallory and Benjamin Castleman.

SUMMARY

An authenticated case of cancer of the breast in a ten-year-old girl is reported.

REFERENCES

1. Eliot, E.: Breast carcinoma in young women. *Ann. Surg.* 53:726, 1911.
2. Levings, A. H.: Carcinoma of the mammary gland in a girl of twelve years old. *Am. J. Surg.* 31:29-32, 1917.
3. Deaver, J. B., and McFarland, J.: *The Breast*. 724 pp. Philadelphia: P. Blakiston's Son & Co., 1917. P. 514.
4. Lee, B. J.: Carcinoma of the breast in the young. *Arch. Surg.* 23:85-116, 1931.
5. Hall, N., and Bagby, J. W.: Carcinoma in the first three decades of life. *J. A. M. A.* 110:703-706, 1938.
6. Kraus, L. W., and Kline, B. S.: Carcinoma of both breasts in a woman under twenty years of age. *Am. J. Surg.* 1:277-280, 1925.

THE TREATMENT OF LOBAR PNEUMONIA WITH SULFATHIAZOLE AND SULFAPYRIDINE*

MORGAN CUTTS, M.D.,† ALEX M. BURGESS, M.D.,‡ AND FRANCIS H. CHAFEE, M.D.‡

PROVIDENCE, RHODE ISLAND

IN AUGUST, 1939, Fosbinder and Walter¹ reported the preparation of sulfathiazole, a derivative of sulfanilamide. Shortly thereafter Rake et al.,²⁻⁴ in a series of articles, reported the results of animal experiments using this new drug, the toxicity of which was in general found to be slightly less than that of sulfapyridine, the principal pathologic change being renal damage. The two drugs were shown to be equally effective against pneumococci. These studies indicated that of the two, sulfathiazole is more rapidly absorbed and excreted. Flippin et al.^{5, 6} confirmed the latter finding in human beings. They also noted that kidney function was depressed in the majority of patients receiving the drug, and that nausea and vomiting was present in only 14 per cent. Long⁷ expressed the opinion that sulfathiazole is approximately as effective as sulfapyridine in the treatment of pneumonia, and that the vomiting is definitely less. He mentioned 1 case of transient anuria and azotemia occurring during its administration. Flippin⁶ has since reported 100 cases of pneumonia treated with sulfathiazole, with good results and no outstanding toxic symptoms.

MATERIALS AND METHODS

The present study deals with 60 patients with lobar pneumonia admitted to the Rhode Island Hospital during the first three months of 1940. Alternate cases received sulfapyridine and sulfathiazole.¶ These two groups were comparable in the average duration of their disease prior to admission, which was three days in both cases. The average of the patients in the sulfapyridine-treated group was fifty-two, as compared with forty-five in those treated with sulfathiazole. The diagnosis was confirmed by x-ray examination in all cases. Eighty per cent of the cases showed typable pneumococci. The sulfathiazole dose was 4 gm. initially, followed by 1 gm. every four hours for forty-eight hours, and thereafter 1 gm. every six hours until resolution was well under way. The dosage of sulfapyridine was similar, except that in most cases the initial dose was 6 gm. Occa-

sionally the sodium salts of both drugs were used intravenously. Other routine measures consisted of blood cultures on admission, frequent determinations of the levels of the drugs in the blood, and oxygen administration when needed. Serum, in adequate dosage, was given to 4 patients receiving sulfapyridine, and to 5 receiving sulfathiazole.

RESULTS

The mortality was 10 per cent in each group. The relation of these deaths to some factors influencing the prognosis is shown in Table 1.

In comparing the temperature drop in response to the two drugs it was found that a prompt fall

TABLE 1. *Prognostic Factors.*

DRUG	NO. OF CASES	DYATHIS	POSITIVE BLOOD CULTURE	PATIENTS OVER 60 Yr.	TYPE 3 CASES	SEVERE TREATMENT
Sulfapyridine..	30	3	3	10	6	4
Sulfathiazole..	30	3	5	4	2	5

occurred in cases treated with sulfapyridine. However, at the end of forty-eight hours approximately the same number were afebrile in the two groups (Table 2).

The increased rapidity of temperature drop in the sulfapyridine group may possibly be related to

TABLE 2. *Antipyretic Effects.*

DRUG	NO. OF CASES	TEMPERATURE WITHIN 24 HR.	FALL TO NORMAL WITHIN 24-48 HR.	TOTALS
Sulfapyridine..	30	10	10	20
Sulfathiazole....	30	5	13	18

the higher blood levels of this drug that we obtained. The average maximum level of sulfapyridine was 6.6 mg. per 100 cc. free and 10.3 mg. total as opposed to 5.2 mg. free and 6.8 mg. total of sulfathiazole. As can be seen from these figures, there is less tendency to conjugation in the case of the latter drug, a fact that has previously been noted by several observers.^{2-4, 7}

Complications were not prominent in either group. Jaundice present on admission and gradually clearing under treatment was noted in 1 case in each group. Empyema and sterile effusion each occurred in 1 case among the patients receiv-

*From the Medical Service, Rhode Island Hospital.

†Assistant visiting physician, Rhode Island Hospital, Providence.

‡Visiting physician, Rhode Island Hospital.

¶The sulfathiazole was supplied through the kindness of Dr. George Harrop, of the Squibb Institute for Medical Research, New Brunswick, New Jersey.

ing sulfathiazole, and sterile effusions were noted in 3 patients given sulfapyridine. The toxic reactions found in the two groups are shown in Table 3.

One difference immediately apparent is the decreased tendency to nausea and vomiting seen with sulfathiazole as compared with sulfapyridine.

TABLE 3. *Toxic Reactions.*

TOXIC SYMPTOMS	SULFAPYRIDINE	SULFATHIAZOLE
Nausea and vomiting.....	18 (60%)	9 (30%)
Drug fever.....	1	2
Red blood corpuscles in urine.....	1	7
Leukopenia.....	0	3
Rise in blood urea nitrogen.....	1	3
Rash.....	0	2

Leukopenia was encountered in 10 per cent of the patients receiving sulfathiazole. In 1 case the white-cell count dropped from 20,000 to 2900 in two days, and in the other two the lowest points reached were 3800 and 1900 respectively. In all three the counts promptly returned to normal on discontinuance of the drug, and there were no related symptoms. A scarlatiniform rash and a papular rash were noted in 2 patients treated with sulfathiazole.

The 4 patients showing a marked rise in blood urea nitrogen during treatment warrant detailed consideration. The only such patient in the sulfapyridine group was a fifty-two-year-old man with an untended pneumonia involving the right lower lobe. He received the usual dosage of drug for five days until a rise in blood urea nitrogen from 22 mg. per 100 cc. on admission to 64 mg. on the fifth hospital day occasioned withdrawal of the drug. During this time the temperature, pulse and respirations were normal, having fallen in the first twelve hours after admission. The patient was receiving adequate fluids. After drug treatment was stopped the blood urea nitrogen fell promptly to 17 mg. per 100 cc. six days later, and he made an uneventful recovery. Blood levels of the drug were high, being 9.8 mg. per 100 cc. free and 14.4 mg. total on the day after the drug was omitted. There was no oliguria. Urine showed a + test for albumin, a few granular casts and a moderately low specific gravity.

The 3 patients receiving sulfathiazole who showed marked increase in the blood urea nitrogen all died, constituting the only deaths in this group. In 1 case the drug could not be implicated. This patient was a seventy-nine-year-old woman with a Type 3 left-lower-lobe pneumonia, who was critically ill on admission and showed signs of spread despite treatment with sulfathiazole and 200,000 units of rabbit serum. She died on the fourth hospital day. The blood urea nitro-

gen was 74 mg. per 100 cc. on the day after admission and rose to 82 mg. twenty-four hours later. One urine specimen showed a + test for albumin. The fluid output was not measured because of incontinence. Sections of the kidneys removed at autopsy showed some arteriolar sclerosis and a few small focal scars consistent with a mild arteriolar nephrosclerosis. There were no significant acute glomerular or tubular changes. In this case high blood levels of the drug were also found, reaching 12.2 mg. per 100 cc. free and 15.9 mg. total.

The second patient was a fifty-seven-year-old man with a Type 18 right-lower-lobe pneumonia, who ran a high fever uninfluenced by the administration of 23 gm. of sulfathiazole and 200,000 units of rabbit serum until death on the twelfth hospital day. The blood urea nitrogen showed a steady increase from 18 mg. per 100 cc. on admission to 139 mg. two days before death, because of which the drug was discontinued on the fifth hospital day. The urinary output had been steadily dropping from the fourth to the seventh hospital day, when the patient developed grossly bloody urine, followed by almost complete anuria. Catheters were passed up both ureters without meeting any obstruction. The two urine sediments examined on admission had been completely normal, and at no time were crystals found in the urine. Blood levels of the drug were high,—up to 10.1 mg. per 100 cc. free and 14.0 mg. total,—with a later shift to the conjugated form after omission of the drug. Unfortunately permission for an autopsy was not obtained.

The third patient was a fifty-one-year-old woman with a right-lower-lobe pneumonia and an admission blood culture positive for Type 14 pneumococcus. Her response to sulfathiazole treatment was immediate, the temperature falling to normal in thirty-six hours and a blood culture becoming sterile. However, the temperature rose again on the eighth hospital day, reaching 106°F., with signs of spread to the other lung. Anuria developed on the eleventh day, the blood urea nitrogen thereafter rising progressively from 12 to 92 mg. per 100 cc. Despite withdrawal of the drug at the onset of anuria, the blood levels of sulfathiazole rose thereafter to 9.1 mg. per 100 cc. free and 13.7 mg. total. Ureteral catheterization was carried out without effect. Coincidentally with the second rise in temperature the patient developed a papular rash over the face, arms and legs. At autopsy there was widespread consolidation of both lungs. The ureters were patent, and the kidneys were soft and reddish. The microscopic changes in the kidneys, examined by Dr. Robert Williams, were as follows:

The glomeruli are everywhere relatively intact. There is extensive fatty metamorphosis of the convoluted tubular epithelium, as shown by epithelial swelling and minute vacuoles throughout the cytoplasm. Here and there in an isolated tubule there is necrosis of the epithelium, sometimes associated with infiltration by polymorphonuclear leukocytes, lymphocytes and large mononuclear cells. This cellular infiltration occurs both within the tubular lumen and in the surrounding interstitial tissue. The collecting tubules are frequently filled with hyaline casts, occasionally with polymorphonuclear leukocytes, and in other places are packed with desquamated epithelium. There is marked lymphocytic infiltration of the wall of the calyx and hyperplasia of its lining epithelium. The epithelium of the tubules at the junction of the cortex and pyramids is frequently packed with granules and aggregates of yellow pigment. The blood vessels are normal.

DISCUSSION

The above results are obviously based on too small a series to be in any way conclusive, but indicate that sulfathiazole is approximately as effective as sulfapyridine in treating pneumococcal pneumonia in man. The slightly more rapid defervescence seen in the majority of the sulfapyridine-treated group certainly cannot be offered as an argument in favor of using this drug in preference to the other. The relative lack of nausea and vomiting in patients treated with sulfathiazole is a definite point in its favor, and the slightly diminished tendency of this drug to conjugation is of at least theoretical advantage.

On a further study of the toxic symptoms, other than nausea and vomiting, will probably depend the ultimate evaluation of the two drugs. Our findings are at variance with other reports in that leukopenia and anuria with uremia occurred with rela-

tive frequency in patients treated with sulfathiazole. The incidence of leukopenia may have been purely accidental, and it is possible that the cases of renal shutdown described above may have resulted from an overwhelming infection with toxic kidney damage, and not from any action of the sulfathiazole. However, none of the patients who died following the administration of sulfapyridine showed any suppression of urine, or uremia. Until more is known of the effect of sulfathiazole on the kidney, it seems obvious that renal function should be watched closely during its administration. In doing this, a study not only of the urine itself but of the daily fluid output and blood urea nitrogen seems essential.

CONCLUSIONS

The results in 30 cases treated with sulfathiazole and a like number treated with sulfapyridine under the same conditions are reported.

The mortality was 10 per cent in each group.

The therapeutic effectiveness and toxic manifestations of the two drugs are discussed.

REFERENCES

1. Fosbinder, R. I., and Walter, L. A.: Sulfanilamide derivatives of heterocyclic amines. *J. Am. Chem. Soc.* 61:2032, 1939.
2. Van Dyke, H. B.; Greep, R. O.; Rake, G., and McKee, C. M.: Observations on the toxicology of sulfathiazole and sulfapyridine. *Proc. Soc. Exper. Biol. & Med.* 42:410-416, 1939.
3. Rake, G.; van Dyke, H. B.; Corwin, W. C.; McKee, C. M., and Greep, R. O.: Pathological changes following prolonged administration of sulfathiazole and sulfapyridine. *J. Bact.* 39:45, 1940.
4. McKee, C. M.; Rake, G.; Greep, R. O., and van Dyke, H. B.: Therapeutic effect of sulfathiazole and sulfapyridine. *Proc. Soc. Exper. Biol. & Med.* 42:417-421, 1939.
5. Reinhold, J. G.; Flippin, H. F., and Schwartz, L.: Observations on the pharmacology and toxicology of sulfathiazole in man. *Am. J. M. Sc.* 199:393-401, 1940.
6. Flippin, H. F.; Schwartz, L., and Rose, S. B.: Comparative effectiveness and toxicity of sulfathiazole and sulfapyridine in pneumococcal pneumonia. *Ann. Int. Med.* 13:2038-2049, 1940.
7. Long, P. H.: Thiazole derivatives of sulfanilamide: sulfathiazole and sulfamethylthiazole. *J. A. M. A.* 114:870, 1940.

REPORT ON MEDICAL PROGRESS

CARDIOLOGY: I. THE MANAGEMENT OF CARDIAC PATIENTS WHO REQUIRE MAJOR SURGERY. II. THE TREATMENT OF CARDIAC ARRHYTHMIAS*

HERRMAN L. BLUMGART, M.D.†

BOSTON

I. THE MANAGEMENT OF CARDIAC PATIENTS WHO REQUIRE MAJOR SURGERY

THE following problems confront the physician when his patient with heart disease develops a condition demanding surgical intervention: Is the diagnosis correct, or are the symptoms and signs due to a cardiac condition requiring medical rather than surgical treatment? In view of the cardiac condition, is the life expectancy sufficient to permit the patient to experience the beneficial results of surgery? What is the additional hazard imposed by the presence of heart disease? Is it such as to present an absolute contraindication to the particular operative procedure? By what means, before, during and after the operation, can the risk be reduced? The knowledge upon which these decisions must be based covers practically the entire domain of medicine and surgery; the close collaboration of surgeon, physician and anesthetist is essential.

It is worthwhile to review in the light of recent contributions two main problems confronting the physician when he considers the advisability of surgery in a cardiac patient. What is the additional hazard imposed by the cardiac condition? How can the stress of operation be minimized by preoperative and postoperative management?

The Increased Hazard of Surgical Operations in Patients with Heart Disease

The patient with heart disease who is not confronted with the necessity of surgical intervention lives constantly under an increased hazard. Knowledge of the degree to which this danger is heightened by operation is essential in weighing the risk of non-interference against the risk of surgical intervention.

The following opinion of Marvin¹ in 1928 has received further support in the intervening years: "For purposes of anesthesia and operation a heart that is damaged but that is carrying on an adequate circulation under normal conditions of life

is the equivalent of a normal heart." The distinction between heart disease and heart failure must be clearly kept in mind.² The added risk due to heart disease is generally proportional to the degree of decrease in the cardiac reserve. Certain conditions are exceptions: syphilitic heart disease with aortic insufficiency, complete heart block as a manifestation of any type of heart disease, aortic stenosis and angina pectoris.^{1,3} Patients with these disabilities are prone to sudden death, and it is consequently impossible to predict the course of events during and after operation. The existence of a considerable risk must be recognized, even though none of the usual contraindications are present.

Patients with congestive failure. The success with which adequate preoperative treatment may convert even those patients with gross evidence of congestive failure into less formidable risks was shown by a group of 144 patients reported by Hamilton.⁴ All had definite signs of congestive failure on entry to the hospital and had major surgical operations; there were but 8 (5.5 per cent) operative deaths. In each case, every effort was made to relieve failure, and when evidence of congestion had disappeared, a further prolonged preparatory period of bed rest was employed. Hamilton advises bed rest whenever possible for at least three weeks after complete subsidence of decompensation, however mild. A similar mortality rate for such patients was reported by Butler, Feeney and Levine.⁵ The presence of adequately controlled, persistent auricular fibrillation did not materially increase the operative risk. Auricular fibrillation and mitral stenosis predispose to the occurrence of embolism, but there is no acceptable evidence that, in the absence of congestive failure, this predisposition is heightened by operation.

Patients with rheumatic heart disease. In patients with mitral stenosis or other evidences of rheumatic fever, past or present, the reactivation of subclinical or latent rheumatic infection by operation or, indeed, by accidents involving fractured bones or sprained joints has been observed.⁶ Subclinical rheumatic fever may be denoted by slight fever, repeated leukocyte counts of above 10,000, elevated heart rate, increase in sedimenta-

*From the Medical Service, Beth Israel Hospital, and the Department of Medicine, Harvard Medical School.

†Associate professor of medicine, Harvard Medical School; visiting physician and director of medical research, Beth Israel Hospital.

tion rate and electrocardiographic changes such as prolongation of the auriculoventricular conduction time. In decisions regarding the most opportune time for elective procedures, this interrelation between operations and activation of rheumatic fever assumes significance.

Patients with angina pectoris or healed myocardial infarction. The recent report by Brumm and Willis⁷ of their experience in 257 cases of coronary arteriosclerosis is a significant contribution. Only those patients were included who had undergone major operative procedures such as cholecystectomy, partial gastrectomy or posterior gastroenterostomy, transurethral prostatic resection, total abdominal hysterectomy or thyroidectomy. Thirty-two of their 257 patients had healed cardiac infarcts at the time of operation; in the remaining cases, angina pectoris had existed for an average of 3.1 years. The majority of these patients with advanced coronary sclerosis and serious surgical conditions were of advanced years, the mean age being 60 years. Half these cases showed significant electrocardiographic abnormalities such as incomplete or complete bundle branch block, complete heart block, auricular fibrillation, or significant T-wave negativity. One hundred cases (39 per cent) had well-marked hypertension.

The degree to which the increased hazard imposed by major surgery in such obviously ill patients can be reduced by skillful medical and surgical care is shown by the fact that only 11 cardiac deaths occurred (4.3 per cent). Seven deaths were due to coronary thrombosis with acute cardiac infarction, and 2 others occurred abruptly without apparent thrombotic occlusion. The authors properly emphasize that their experience should not instill false optimism, since the low incidence of fatality resulted from careful preoperative study, judicious selection, expert administration of anesthetics and skillful surgery. Operation was confined to those cases presenting unmistakable indications. The authors caution that it is of paramount importance that the surgeon insist on limiting the operation to the procedure planned in advance and avoid undertaking additional operative steps that might be justifiable in a patient without heart disease.

Surgery in relation to acute myocardial infarction. Patients with acute manifestations of coronary disease are poor operative risks, and surgery should not be undertaken except in extreme emergencies. Necessary operations may be performed, however, about three months following acute myocardial infarction when the patient is ambulatory and the infarct has apparently completely healed. According to the studies of Mallory, White and Salcedo-Salgar,⁸ the healing proc-

ess may usually be considered complete by that time.

Postoperative coronary thrombosis is one of the complications that cardiac patients, especially those in the older groups, may develop. This extremely dangerous complication dispels any optimistic view regarding recovery from the operation and demands the most painstaking care. A recent study by Master, Dack and Jaffe⁹ lends support to the belief that operations may precipitate attacks of postoperative thrombosis. The authors have found several strong reasons for this opinion. It is apparent from their study that, emergencies excepted, if operation is to be undertaken in patients over fifty years of age, the cardiac status should be carefully appraised, and that when operation is considered advisable, special care must be taken to minimize shock and dehydration and to avoid infection. That shock following operations, hemorrhage and other states may precipitate acute coronary occlusions is further supported by a recent clinical and pathologic study of 350 consecutive, unselected, necropsied patients.¹⁰ Eleven cases of multiple fresh coronary occlusions and 38 cases of single fresh coronary occlusions were found. Shock, with its attendant fall in blood pressure, dehydration and so forth, appeared to be a precipitating factor in all cases of multiple fresh coronary occlusions and in half the cases of single fresh occlusions; operation and its complications were responsible for shock in a significant number.

Since the introduction of insulin in the treatment of diabetes, the arteriosclerotic complications of that disease have become the chief cause of death in diabetes. The high incidence of acute coronary thrombosis in diabetic patients has been pointed out by several authors.^{11, 12} It is therefore wise for the physician to warn surgeons contemplating operation on older diabetic patients, both male and female, of the possibility of precipitating an attack of coronary thrombosis and the importance of avoiding shock or a fall in blood pressure from any cause. The dangers of hypoglycemia in precipitating acute myocardial infarction in such patients should be particularly kept in mind.

Preoperative and Postoperative Management of Cardiac Patients

The frequency with which immediate operation is considered necessary has declined greatly in recent years. In the vast majority of cases an opportunity for preoperative preparation of the patient is available.

Sedation. The preoperative use of barbiturates such as phenobarbital in $\frac{1}{4}$ -gr. or $\frac{1}{2}$ -gr. doses three or four times daily to lessen apprehension and its effects on the cardiovascular system has

won widespread adoption. Larger doses, such as $1\frac{1}{2}$ to 3 gr. of phenobarbital, Sodium Amytal or Pentobarbital the evening before operation, and again immediately prior to operation, are commonly administered. Not infrequently, however, when the larger doses are given and particularly when morphine is also administered, the synergistic effect of a general anesthetic may result in dangerous consequences during the course of the operation. Delayed absorption of medication by mouth may cause the action of the drug to appear during operation, with anoxemia and resulting arrhythmias or vasomotor collapse.

In the administration of sedatives, sufficient dosage should be employed to produce drowsiness; narcosis, however, is to be avoided. The use of the smaller rather than the larger dose of the barbiturates mentioned above is usually advisable. If the patients are still alert or nervous immediately before operation, $\frac{1}{2}$ or $\frac{1}{4}$ gr. of morphine may be injected subcutaneously.

When sedatives or opiates are administered for the first time, one occasionally discovers the presence of an idiosyncrasy, the patient becoming excited instead of drowsy. Since some cardiac patients will not withstand complications that more normal subjects might easily surmount, such untoward and even dangerous occurrences must be avoided by administering, whenever possible, several days before operation, test doses of all medicines that are to be used during the immediate preoperative and postoperative course. This procedure will make it possible to observe the nature of the reaction and gauge the optimum dosage with minimum hazard to the patient.

Body fluids and electrolytes. The full significance of the dehydration that may result from insensible loss of water, from vomiting and diarrhea and from other causes has been appreciated only in recent years through the observations of Gamble and his associates¹³ and of Collier and Maddock.¹⁴ The nature and amounts of fluid to be administered, which have been discussed elsewhere in this series of reports,¹⁵ should result in an output of urine of at least one liter a day.

Cardiac patients are all too frequently subjected to vigorous diuretic medication with restriction of salt and fluids before operation, only to receive, according to routine orders a few hours later, large quantities of saline solutions by vein or by hypodermoclysis. *No specific routine can be followed in respect to cardiac patients.* If, despite treatment before operation, slight congestion of the lungs and evidences of edema are still present, the physician may properly consider that the patient has somewhat more than the normal available re-

serves of electrolytes and fluid that may be utilized in replacing the loss occasioned by operation. The findings on physical examination, the amount of perspiration, the amount of urinary output and the subjective degree of thirst experienced by the patient are important guides in deciding the amount of fluid to be administered. If the administration of fluids is indicated, the avoidance of heavy sedation and prolonged narcosis may enable the patient to take the necessary fluids by mouth, thereby eliminating the pain and discomfort of hypodermoclysis and the resultant effects on the cardiovascular and central nervous systems.

If fluids are given intravenously, the amounts and the rate at which they are introduced must be carefully supervised. The occurrence of pulmonary edema and of angina pectoris in cardiac patients as a result of the intravenous administration of fluids is not rare. An abnormally great and prolonged rise in venous pressure following the injection of 1500 cc. of normal saline at a rate of approximately 50 cc. a minute has been observed in patients with heart disease.¹⁶ Postoperative studies of the dynamics of the circulation in patients without heart disease have shown that if 500-1500 cc. of physiological saline, or 5 per cent glucose solution in physiological saline are injected at rates of less than 20 cc. a minute, very slight changes in the cardiovascular functions result.¹⁷ The blood volume is usually somewhat increased. When intravenous administration of fluids to cardiac patients is indicated, rates of less than 15 cc. a minute avoid these unnecessary hazards. Aside from their immediate effect, intravenous infusions that continue or are repeated over a period of several days, as may be necessary after prostatectomy, favor the development of edema, both peripheral and pulmonary, even though the fluid is given at very slow rates. The lowering of the plasma-protein level, due to plasma dilution, vasodilatation due to increased blood volume, and the tendency toward increased venous pressure by operating together over a period of days, may result in clinically perceptible edema.¹⁷ Postoperative nutritional edema may favor such an occurrence.¹⁸

Digitalis. The almost routine digitalization of patients over the age of fifty has received diminishing acceptance. No trustworthy evidence indicates that any useful purpose is served thereby in patients who do not have congestive heart failure or auricular fibrillation. In general the same indications for digitalis apply to the preoperative cardiac patient as to the cardiac patient in whom surgery is not contemplated. In patients with auricular fibrillation, somewhat greater than usual

amounts may be employed because of the disproportionate rise in ventricular rate that may occur under stress.¹⁹

Anesthesia. The anesthetist is to be considered as a consultant rather than as a technician and should participate in discussions of the particular problems offered by the individual patient. Precautions should be undertaken to prevent atelectasis. Large doses of narcotics before and after operation are undesirable, and atropine should be used only in small doses or omitted entirely from the preoperative medical regime. To protect the liver against the fat-solvent anesthetic agents and to prevent general anoxia with its deleterious cardiovascular effects, the use of a high percentage of oxygen with the inhalation of anesthetics is advantageous.²⁰ The judicious use of preoperative sedation reduces the concentration of gaseous anesthetics necessary for a given level of anesthesia and thereby permits higher concentrations of oxygen to be used simultaneously.²¹ The use of nitrous oxide anesthesia is particularly hazardous in cardiac patients for operations of long duration because of the frequency of anoxia. The newer developments in the administration of spinal anesthetics have increased the applicability of this form of anesthesia. The danger of a fall in blood pressure, particularly in patients with marked hypertension, should be kept in mind. While statistics indicate that postoperative pulmonary complications are more frequent in patients after spinal anesthesia, this result can be attributed in part to the fact that spinal anesthesia usually is reserved for the elderly subjects with pulmonary disease. With these considerations in mind, the choice of anesthesia for the cardiac patient is much the same as for the non-cardiac patient; ether continues to be the most widely used anesthetic. Operation during the late hours of the morning or even in the afternoon may be advantageous in elderly cardiac patients with coincident pulmonary bronchiectasis, who raise considerable amounts of sputum on awaking in the morning.

Oxygen. Prophylactic oxygen therapy should be considered after operation in all cases in which the cardiac reserve is limited. With modern simplified methods of oxygen therapy, such as the B.L.B. mask and the face tent, oxygen can be used economically and more satisfactorily than formerly.²² Apprehension may be minimized by administering oxygen preoperatively to such patients for short periods of time to accustom them to this procedure.

Nitroglycerin. The prophylactic use of nitroglycerin has not been so widely utilized as it deserves.²³ The patient with angina pectoris whose

attacks respond to this medication may benefit greatly by receiving 1/500 gr. under the tongue every half hour preoperatively, and if the operation is to be done with local anesthesia, during operation as well.

Prevention of Postoperative Complications in Cardiac Patients

Particular consideration must be given to certain complications which are especially prevalent in cardiac patients.

Pulmonary complications. The incidence of these justly dreaded complications can be reduced by the following measures: eliminating pulmonary congestion of lungs, preoperatively; obviating prolonged narcosis; avoiding the administration of unduly large amounts of fluids postoperatively or of unnecessarily large doses of sedatives; removing bronchial secretions with a catheter or the use of postural drainage in certain cases; frequent changing of the position of the patient; encouraging deep breathing; and avoiding tight abdominal binders and distention. In all patients with heart disease and especially those who have a limitation in their cardiac reserve, a decreased incidence of pulmonary embolism is believed to have been accomplished by massage and by active and passive motion of the limbs. The use of helium and oxygen mixtures, first introduced by Barach in 1934, has received favorable comment when used in the occasional instances of obstruction to the passage of air in the respiratory passages.²² Oxygen therapy should be used more freely for any postoperative complication occurring in cardiac patients. Morphine lowers both the rate and amplitude of respiratory excursions; its use in doses that usually cause no ill effects may lead to atelectasis and bronchopneumonia in the elderly cardiac patients with pulmonary emphysema.

Intestinal distention. Cardiac patients are especially prone to develop intestinal distention. The inhalation of pure oxygen as suggested by Fine and Starr²⁴ will not only benefit the intestinal distention, but will also tend to obviate anoxemia and its effects on the heart. Intractable distention in these patients may occasionally justify the use of an inlying Levin tube with suction applied.

Malnutrition. Cardiac patients not infrequently manifest hypoproteinemia as a result of anorexia, albuminuria and the dilution of the blood plasma that accompanies congestive failure. Blood protein may assume normal values after diuresis in some cases. It should be remembered that in the presence of an increased capillary permeability such as may accompany congestive failure, the administration of large quantities of saline solutions may result in great harm. The use of a well-balanced

diet and the transfusion of plasma or blood are effective. The importance of normal nutritional reserves and the particular effect of thiamin deficiency on the heart must be kept in mind.²⁵

Cardiac complications. The incidence of acute myocardial infarction and the occurrence of shock, dehydration or fall in blood pressure from any cause as a contributing factor have already been discussed. The effectiveness of Paredrine²⁶ and other sympathomimetic drugs in preventing hypotension in the course of spinal anesthesia and in restoring the blood pressure to normal levels in the treatment of peripheral vasomotor collapse has been reported. Doses of 10 mg. given intramuscularly, and repeated according to the effect on blood pressure, are to be recommended. Unlike amphetamine (Benedrine), Paredrine does not cause psychic stimulation, and in contrast with ephedrine, no increase in the output of the heart occurs. Untoward effects on the heart are not caused by therapeutic doses.²⁶

Paroxysmal auricular and ventricular tachycardia, auricular fibrillation and various degrees of heart block may occur during operation. Although cardiac arrhythmias frequently occur in patients without heart disease, there is a greater incidence among those with abnormal hearts. The treatment of these disorders will be discussed later.²⁷

Drugs Commonly Used Preoperatively and Postoperatively That May Affect the Heart Adversely

Certain medicinal agents, commonly used in the postoperative treatment of patients, have additional effects on the cardiovascular system that may lead to dangerous or even disastrous consequences. Aside from sedatives and other agents discussed elsewhere in this report, the following may be cited:

Extracts of the posterior lobe of the pituitary gland (Pituitrin, Pitressin and so forth). When these are used for treating abdominal distention they may, through vasoconstrictor action, precipitate severe angina pectoris and collapse. In cardiac patients with intestinal distention and oliguria, Pituitrin is not infrequently given for the intestinal distention, without a realization that it likewise tends to accentuate the oliguria.

Carbon dioxide mixtures. The inhalation of such mixtures invoked because of intractable hiccough, particularly after genitourinary operations, imposes a strain on the heart, since the ventricular rate is increased and the blood pressure and minute volume output of the heart become somewhat elevated, particularly if concentrations of more than 5 per cent are utilized.²⁸

Ergot. The administration of ergot to produce uterine contraction after dilatation and curettage not infrequently leads to severe cardiac pain.

Atropine sulfate. When atropine sulfate is used to lessen the bronchial and upper respiratory secretions, it is not always realized that, through the inhibitory effect on the vagus nerves, undue elevation of the ventricular rate may occur, particularly in patients with auricular fibrillation.

Insulin. Degrees of hypoglycemia that would be tolerated readily by most patients may precipitate the characteristic manifestations of acute myocardial infarction in the presence of coronary arteriosclerosis.

Adrenalin. Particularly in patients with angina pectoris due to coronary arteriosclerosis, and even in the presence of asymptomatic coronary narrowing or occlusion, adrenalin may incite severe cardiac pain and occasionally may produce collapse and death.

Cocaine and novocain. The ready absorption of cocaine and novocain when applied to the upper respiratory passages may cause the inception of collapse or of cardiac arrhythmias, and at times of ventricular fibrillation and death. This danger is present in normal persons, but particularly in patients with an irritable myocardium resulting from the reduction in coronary blood flow by coronary arteriosclerotic lesions.

The use of these agents is not necessarily contraindicated in patients with heart disease; a realization of their effects on the cardiovascular system and the possible hazards involved will suffice to prevent their indiscriminate and unwise employment when their beneficial effects are desired.

II. THE TREATMENT OF CARDIAC ARRHYTHMIAS

Disorders of cardiac rhythm constitute one of the most frequent conditions that confront the physician. Knowledge of the precise mechanisms of the various arrhythmias is essential; although certain irregularities may be regarded with equanimity and may require no treatment, others necessitate specific therapy, since they interfere with the well-being of the patient and may even threaten his life. The action of the drugs to be used must be understood, since medication which terminates one arrhythmia may be ineffective or even dangerous in another.

The most important types of cardiac arrhythmias are as follows:

Extrasystoles, auricular or ventricular
Paroxysmal auricular tachycardia

Paroxysmal ventricular tachycardia
 Auricular flutter
 Auricular fibrillation
 Heart block with Adams-Stokes attacks

Drugs that exert a useful effect are as follows:

Quinidine
 Digitalis
 Acetyl-beta-methylcholine (Mecholyl)
 Emetics, such as syrup of ipecac

The clinical recognition, electrocardiographic characteristics, and the mechanism of the various arrhythmias are clearly delineated in the various cardiological texts. Several reports have clarified certain aspects of these conditions and will be summarized. Gold²⁹ states that although a differential diagnosis of the various arrhythmias can be made solely by clinical means, an electrocardiogram is usually necessary to establish the diagnosis and to ensure safe and effective treatment. The routine tracing may fail to be of value; however, a tracing should be made *before* and *during* carotid-sinus pressure. A patient with a rapid regular tachycardia of 150-175 a minute may have either sinus tachycardia, paroxysmal auricular tachycardia, auricular flutter or ventricular tachycardia. The standard tracing may be equivocal; the auricular deflections may be buried in the ventricular deflections. Application of carotid-sinus pressure may clarify the diagnosis. If auricular and ventricular contractions are slowed, the diagnosis of sinus tachycardia is evident. If both auricle and ventricle are brought to a complete momentary standstill, the diagnosis of paroxysmal auricular tachycardia may be confirmed. If auricular flutter is present, the ventricular rate may be slowed, and the auricular deflections of 300 or more a minute may be readily seen. Carotid-sinus pressure may produce no effect on either the auricle or ventricle, in which case, and in the presence of other characteristics of the ventricular deflections, a diagnosis of ventricular tachycardia is indicated. If carotid-sinus pressure is not effective, ocular pressure, holding the breath at the end of deep inspiration, straining at the end of deep inspiration with the glottis closed, or lying across the bed with the head hanging over the side of the bed, may be of assistance.

Extrasystoles

This, the commonest of all cardiac irregularities, frequently occurs unassociated with organic heart disease in nervous, apprehensive patients. In occasional cases, when numerous extrasystoles mask the underlying sinus rhythm, differentiation from auricular fibrillation may be difficult without the aid of the electrocardiograph. Reassurance, the

prescription of a rational regime of life, psychotherapy, the avoidance of tobacco, tea and coffee, and the administration of repeated small doses of sedatives are frequently effective. In refractory cases, quinidine sulfate, 3.0-5.0 gr., on awaking and every hour or five hours until bedtime is to be recommended. Extrasystoles of ventricular origin may predispose patients with coronary arteriosclerosis to attacks of paroxysmal ventricular tachycardia; quinidine should be employed. Although digitalis in such patients may increase myocardial irritability and hence increase the number of extrasystoles, in others the favorable effect on the heart results in abolition of the extrasystolic irregularities. Partial digitalization by relatively small doses, such as 1.5 gr. two or three times daily, with careful observation of the results of treatment, is advisable under such circumstances. The use of repeated small doses of the barbiturates, such as phenobarbital, $\frac{1}{4}$ gr. three or four times daily, is a valuable adjunct.

Paroxysmal Auricular Tachycardia

This arrhythmia frequently occurs in the absence of organic heart disease, is sudden in onset, lasts a few seconds to hours or even days and is characterized by its extraordinarily constant rate of 150-200 a minute. If the attacks are short and infrequent, no treatment is necessary. Carotid-sinus pressure, or one of its equivalents, previously mentioned, may terminate the attack if spontaneous subsidence does not occur. Since the attacks frequently cease spontaneously and are greatly influenced by emotional states, the physician attending a patient early in the attack should defer vigorous therapy and prescribe sedation, such as 5.0 gr. of barbital, 3.0 gr. of Sodium Amytal or 15-gr. tablet of triple bromides, to be followed by smaller doses in two or three hours until drowsiness occurs. If the attack persists, Mecholyl (acetyl-beta-methyl-choline), the most effective drug for this condition, may be administered, provided, however, bronchial asthma, angina pectoris, hyperthyroidism³⁰ or recently healed myocardial infarction is not present. Mecholyl is a powerful parasympathetic stimulant and not uncommonly produces flushing, salivation, profuse perspiration, nausea, vomiting and occasionally dyspnea, precordial pain or collapse. Because of these severe untoward reactions, cautious administration must be practiced. The patient should be recumbent during and immediately after the injection. Since Mecholyl is such a powerful agent and may cause drastic toxic reactions, it should never be given until a second syringe containing 1/50 or 1/100 gr. of atropine has been prepared and is immediately available. Atropine is an instantaneously effective

tive antidote. Certain authorities advise intramuscular injection of atropine, but intravenous administration is usually preferable. Mecholyl should be injected subcutaneously or, in resistant cases, intramuscularly; *intravenous injection is extremely dangerous and should never be practiced*. An ampoule of Mecholyl Hydrochloride usually contains 25 mg.; this is dissolved in 0.5 or 1.0 cc. of water. The dosage is proportional to age and body weight. The average dose is 25 mg.; 10 to 20 mg. may suffice for patients ten to twenty years of age, whereas 50 or 60 mg. may be necessary in older, obese persons. The effect of the dose may be enhanced by vigorously massaging the area of injection and by applying carotid-sinus pressure from time to time.³¹ Abrupt cessation of the attack should occur within fifteen minutes. A second or even third injection may be necessary at fifteen-minute to twenty-minute intervals. If the dosage is too large, the heart may manifest complete standstill for thirty or forty-five seconds.

Quinidine is antagonistic to Mecholyl, and if the patient has taken any quinidine within twenty-four hours of the time Mecholyl is given, the latter may fail even if the dose is larger than that ordinarily employed.³²

If the use of Mecholyl is not considered advisable, emetics, such as syrup of ipecac in doses of 1 or 2 teaspoonfuls, may be used.³³ If the desired therapeutic result is not obtained, the dose may be repeated after one hour. Nausea and vomiting with their associated vagal activity usually terminate the attack of tachycardia. Apomorphine, 1/20 gr. by subcutaneous injection, has been suggested and not infrequently will accomplish the same result, but it must be considered a drastic measure.

Quinidine, in large doses (10 gr.) by mouth every two hours until a total of 30, 40 or even 50 gr. has been given, is often employed. Similarly, 7½ gr. of quinine dihydrochloride injected intravenously or intramuscularly after dilution with 20 cc. of fluid has been utilized. The toxicity of such large doses and the uncertainty of success have led to a less frequent use of quinine and its derivatives. Large doses of digitalis, although occasionally effective, are usually unsatisfactory.

Prevention of attacks of paroxysmal auricular tachycardia. Some patients are troubled by frequent recurrent attacks of tachycardia. Digitalis is frequently effective when full dosage is employed. If the patient has not received digitalis within ten days, 3.0 gr. may be given at six-hour intervals for three or four doses, and then 1.5 gr. two or three times daily until evidence of digitalization appears, such as anorexia or T-wave changes, following

which a maintenance dosage should be employed. If digitalis is not effective, it should be discontinued, and quinidine sulfate should be prescribed in doses of 5.0 gr. on awaking and then every four or six hours until bedtime. If the patient is hypersensitive to quinidine or shows idiosyncrasies, such as diarrhea or nausea, the dosage should be decreased or the drug discontinued. The use of sedatives, psychotherapy and the avoidance of fatigue are important. The possibility of thyrotoxicosis must be considered.

Paroxysmal Ventricular Tachycardia

This disorder, although it is distinctly uncommon, is a serious condition, must be promptly recognized and must be treated with dispatch. Although far less frequent than paroxysmal auricular tachycardia, paroxysmal ventricular tachycardia is more commonly associated with serious myocardial disease, such as acute infarction, and may lead to ventricular fibrillation and death. The development of ventricular fibrillation is favored by digitalis, and the use of this drug is therefore definitely contraindicated.

Quinidine is effective and should be employed until toxic or therapeutic effects are evident. Because of the seriousness of the condition, it is usually advisable to begin with a dose of 10 gr. Its effect will be evident in two hours, at which time the dose can be repeated or increased. Larger and more frequent doses, although entailing a risk, may be indicated in desperate circumstances. Fahr³⁴ reports using as much as 5.5 gr. in five hours in one case. Dangerous defects of intraventricular conduction may occur; frequent electrocardiograms taken during treatment should be helpful in avoiding such complications.

In paroxysmal auricular tachycardia, the auricular rate remains remarkably constant until the abrupt lowering to normal. In paroxysmal ventricular tachycardia, however, the ventricular rate may vary several beats a minute. Quinidine may lower the ventricular rate, even though it does not abolish the abnormal rhythm. This is important, since, in cases with a ventricular rate approaching 200 or more, severe precordial pain or collapse may be experienced. Under such circumstances, lowering of the rate may dispel the pain, reduce the work of the heart and tend to prevent cardiac damage and the onset of ventricular fibrillation. Since this effect is related to the concentration of quinidine within the body, doses of 5.0 to 7.5 gr. of quinidine should be repeated every two hours, the ventricular rate and clinical condition serving as guides, until the therapeutic effects are attained or nausea, vomiting and so forth make lessening of the dosage imperative.

In the presence of vomiting or circulatory collapse, poor absorption from the gastrointestinal tract makes parenteral therapy advisable; quinine dihydrochloride may be used under such conditions.³⁵

The prophylactic use of quinidine is indicated in patients with acute myocardial infarction who develop multiple ventricular premature beats. Similarly, in certain persons who are prone to develop recurrent attacks of paroxysmal ventricular tachycardia, quinidine in doses of 5.0 gr. administered four times daily is frequently effective.

Auricular Flutter

The auricle in this infrequent condition beats at a rate of 250–350 a minute as a result of waves circulating in a ring of muscle between the superior and inferior venae cavae. The rate of beating of the auricles is extraordinarily constant. The ventricular rate is frequently half that of the auricles, but may vary from time to time; in fact, an abrupt rise in ventricular rate due to a change from 4:1 to 3:1 or 2:1 block on slight effort may be of diagnostic importance. Quinidine and digitalis are the two effective drugs in the treatment of this disorder. Most authorities advise the initial use of quinidine alone. Large doses are usually required—10 gr. every two hours for three to five doses are sometimes necessary. In the presence of rapid ventricular rates, however, digitalis should be utilized. By imposing auriculoventricular block, the ventricular rate may be controlled at normal levels, even though the flutter of the auricles persists. The dosage may be similar to that employed in paroxysmal auricular tachycardia. In some cases neither quinidine nor digitalis abolishes the arrhythmia, but the patient may continue a comfortable and normal life, with the ventricular rate satisfactorily controlled by digitalis.

The administration of digitalis frequently converts auricular flutter to auricular fibrillation. Normal sinus rhythm may occur spontaneously on withdrawal of digitalis or following the administration of quinidine.

In certain patients prone to recurrent attacks, quinidine may be useful when administered according to the plan outlined for patients with recurrent attacks of paroxysmal ventricular tachycardia.

Auricular Fibrillation

The indications and contraindications for the use of quinidine in restoring normal rhythm in patients with auricular fibrillation continue to be subject to a wide diversity of opinion. In general it has become increasingly clear that the abolition of auricular fibrillation by quinidine has very limited application; auricular fibrillation of long standing, cardiac enlargement, advanced mitral steno-

sis, active rheumatic infection and prior congestive failure contraindicate its use. Patients with persistent auricular fibrillation are better stabilized and more safely controlled by appropriate dosage of digitalis. The urgency of the situation will influence the speed with which the patient is digitalized; the plan of treatment is usually similar to that described above for the prevention of attacks of paroxysmal tachycardia.

In some patients after subtotal thyroidectomy for thyrotoxicosis, and in some with paroxysmal auricular fibrillation in the absence of congestive heart failure or organic heart disease, quinidine may be useful to abolish or prevent auricular fibrillation. If no idiosyncrasy to quinidine is manifest after a test dose, the drug may be administered in three doses of 5.0 gr. each every two or three hours for one day, giving four and then five or six doses on each succeeding day.

Complete Heart Block with Adams-Stokes Attacks

Most cases of complete heart block require no treatment, although digitalis is frequently given because of its beneficial effect on the myocardium. Occasionally patients suffer syncopal attacks when transitions from partial to complete block occur. Digitalis will maintain complete block and prevent such syncopal attacks. In a second group of cases, syncopal attacks occur in the presence of persistent complete heart block. In these patients the symptoms are due to a lowering of the idioventricular rate from 30 or 40 to 9 or 10 a minute.³⁹ Ephedrine in doses of $\frac{3}{8}$ gr. four times a day may be effective. In some cases emotional factors are responsible for changes in the degree of block and thus give rise to Adams-Stokes attacks. Phenobarbital, in doses of $\frac{1}{4}$ gr. four times a day, may be more effective in preventing attacks in such patients than is digitalis, ephedrine or adrenalin.

330 Brookline Avenue

REFERENCES

1. Marvin, H. M.: The heart during anesthesia and operative procedures. *New Eng. J. Med.* 199:547-551, 1928.
2. Sprague, H. B.: The heart in surgery: analysis of results of surgery on cardiac patients during past 10 years at the Massachusetts General Hospital. *Surg., Gynec. & Obst.* 49:54-58, 1929.
3. Marvin, H. M., and Sullivan, A. G.: Clinical observations upon syncope and sudden death in relation to aortic stenosis. *Am. Heart J.* 10:725-735, 1935.
4. Hamilton, B. E.: Congestive heart failure and angina pectoris in surgical patients. *S. Clin. North America* 6:637-650, 1926.
5. Butler, S.; Feeney, N., and Levine, S. A.: The patient with heart disease as a surgical risk: review of four hundred and fourteen cases. *J. A. M. A.* 95:85-91, 1930.
6. Bland, E. F., and Jones, T. D.: Clinical observations on the events preceding the appearance of rheumatic fever. *J. Clin. Investigation* 14:633-648, 1935.
7. Brumm, H. J., and Willius, F. A.: The surgical risk in patients with coronary disease. *J. A. M. A.* 112:2377-2380, 1939.
8. Mallory, G. K.; White, P. D., and Salcedo-Salgar, J.: The speed of healing of myocardial infarction: a study of the pathologic anatomy in seventy-two cases. *Am. Heart J.* 18:647-671, 1939.
9. Master, A. M.; Dack, S., and Jaffe, H. L.: Postoperative coronary artery occlusion. *J. A. M. A.* 110:1415-1418, 1938.
10. Blumgart, H. L.; Schlesinger, M. J., and Zoll, P. M.: Multiple fresh coronary occlusions in patients with antecedent shock. *Arch. Int. Med.* (in press).
11. Root, H. F.; Bland, E. F.; Gordon, W. H., and White, P. D.: Coronary atherosclerosis in diabetes mellitus: a postmortem study. *J. A. M. A.* 113:27-30, 1939.

- 12 Vander Veer, J. B. Symposium on metabolic diseases the cardiovascular complications of diabetes mellitus *M Clin North America* 23 1561 1574, 1939
- 13 Gamble J. L. *Chemical Anatomy Physiology and pathology of extra cellular fluid* 52 pp. Privately printed under the auspices of the Department of Pediatrics Harvard Medical School 1939
- 14 Maddock W. G., and Collier, F. A. Water balance in surgery *J A M A* 108 16, 1937
- 15 Butler A. M. Electrolyte and water balance *New Eng J Med* 220 827 834 1939
- 16 Richards D. W., Jr. Caughey J. L., Courmand A. and Chamberlain F. L. Intravenous saline infusion as a clinical test for right heart and left heart failure *Tr A Am Physicians* 52 250 258 1936
- 17 Altschule M. D., and Gilligan D. R. The effects on the cardiovascular system of fluids administered intravenously in man II The dynamics of the circulation *J Clin Investigation* 17:401-411 1938
- 18 Jones C. M., and Eaton F. B. Postoperative nutritional edema *Arch Surg* 27 159 177, 1933
- 19 Blumgart H. L. The reaction to exercise of the heart affected by auricular fibrillation *Heart* 11 49 56 1924
- 20 Blalock, A. General principles of preoperative and postoperative treatment *Arch Surg* 40 1039 1043 1940
- 21 Robbins B. H. Preanesthetic medication *Arch Surg* 40 1044 1056, 1940
- 22 Boothby W. M., Mayo, C. W., and Lovelace W. R. II The use of oxygen and oxygen-helium with special reference to surgery *S Clin North America* 20 1107 1168 1940
- 23 Riseman J. E. F. and Brown M. G. Medicinal treatment of angina pectoris *Arch Int Med* 60 100-118 1937
- 24 Fine J. and Starr, A. Intestinal distention *Res Cas roentgenol* 6 419 422 1939
- 25 Weiss S. and Wilkins R. W. Disturbance of the cardiovascular system in nutritional deficiency *J A M A* 109 86 93 1937
- 26 Altschule M. D. and Iglaue, A. The effect of benzedrine (B phenyl ethyl amine hydrobromide) on ration in normal man *J Clin*
- 27 Kurtz C. M. Bennett J. H. and studies during surgical anesthesia
- 28 Grollman A. Physiological variations in cardiac output of man the effect of breathing carbon dioxide and of voluntary forced ventilation on the cardiac output of man *Am J Physiol* 94 287 299, 1930
- 29 Gold H. Treatment of cardiac arrhythmias *M Clin North America* 24 577 593 1940
- 30 Nahum L. H. and Hoff H. L. Auricular fibrillation in hyperthyroidism *Am J Physiol* 94 287 299, 1930
- 31 St. action cardiac
- 32 Ac
- 33 Weiss S., and Sprague H. B. Vagal reflex irritability and the treatment of paroxysmal auricular tachycardia with ipecac *Am J M Sc* 154 53 63 1937
- 34 Fahr G. The treatment of cardiac irregularities *J A M A* 111 2263 2275 1938
- 35 Riseman, J. E. F. and Linenthal, H. unpublished data

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 26451

PRESENTATION OF CASE

A forty-two-year-old insurance broker entered the hospital complaining of a chronic cough and chest pain.

The patient felt perfectly well until eight weeks before admission, when he contracted a slight cold that cleared within a few days. One week later he suddenly noticed a sharp pain in the anterolateral portion of the left lower chest. His physician said that he had a cold, but the pain continued and within the next three days a cough with yellow sputum developed. Another physician made a diagnosis of bronchitis, put him to bed, and treated him with sulfapyridine. The symptoms continued, however, and the temperature rose to 101.4°F. Physical examination at that time showed a decrease in respiratory movement on the left, with inability to take a deep inspiration because of pain in the left lower chest that radiated to the adjacent upper quadrant of the abdomen. On this side there was dullness to percussion in the lower half, both anteriorly and posteriorly, and breath sounds were absent over these areas. X-ray examination revealed an irregular consolidation of the lower two thirds of the left lung; the tracheal and heart shadows were displaced to the right. The urine was normal, and the white-cell count 8500. Nothing was obtained on two pleural punctures. A diagnosis of unresolved pneumonia was made, and the patient was admitted to another hospital. Two weeks later the temperature had returned to normal, and x-ray study showed only a small area of consolidation in the left lower chest. He was about to be discharged, when the temperature rose again and continued in an irregular spiking manner finally steadying so that it was 100°F. each morning and 101 each afternoon. Several sputum examinations and one gastric lavage were negative for tubercle bacilli. On the thirty-sixth day of hospitalization and two days before he entered this hospital, the patient was referred to another institution for diagnosis. Here a bronchoscopic examination was performed, and abnormal findings were reported as follows:

Mucopurulent secretions were encountered in the left stem bronchus and were aspirated. The upper-lobe orifice appeared normal, but the lower-lobe orifice, as well as the lower-lobe bronchus, was narrowed concentrically so that it was impossible to pass the full lumen of an S-40 bronchoscope; the diameter of this bronchus was reduced by 25 per cent. The mucosa of the bronchus was intact, although slightly reddened and edematous. The secondary divisions of the bronchus were visualized, and no neoplastic tissue was evident.

The patient was referred to this hospital. At the time of admission he had had no chest pain for three weeks and the cough and sputum, although still present, had improved greatly. He had lost about 20 pounds since the onset of the illness.

The patient had had the usual childhood diseases, including diphtheria at seven years. The family history was irrelevant.

Physical examination showed a well-developed and well-nourished man in no apparent distress. Examination of the heart was negative; the blood pressure was 115 systolic, 70 diastolic. There was no apparent diaphragmatic excursion. Dullness to percussion and diminished breath sounds were noted at the left lung base posteriorly, and fine rales were heard along the eighth, ninth and tenth ribs at the posterior axillary line. The physical findings were otherwise negative.

Examinations of the urine were negative. Examination of the blood showed a red-cell count of 4,960,000 with a hemoglobin of 11.9 gm. (photoelectric-cell technic), and a white-cell count of 21,500. The sedimentation rate was 55 mm. in one hour. The nonprotein nitrogen of the blood serum was 15 mg. per 100 cc. and the serum protein 6.9 gm. A blood Hinton test was negative. Microscopic examination of the sputum on three occasions failed to show tubercle bacilli. One of three sputum cultures grew a few colonies of beta hemolytic streptococci; the remaining two yielded the usual bacteria of the respiratory tract.

A fluoroscopic examination showed the left side of the diaphragm to be fixed, irregular and high. A shifting fluid level in the region of a sharply defined hemispherical shadow occupied the lateral aspect of the left base. This shadow was continuous with that of the diaphragm, and density in the region of the pleura simulated fluid. Two gas bubbles were present that shifted in position, one lying within the hemispherical shadow and the other just above and anterior to it. The bubble outside the hemispherical shadow was not seen in all the films, but the one within the hemispherical shadow increased in size after postural drainage. The sharply defined shadow was apparently a cavity, the walls of which varied from 4 to 10 mm. in

thickness. The heart was slightly displaced to the left, and a dense irregular shadow was seen along its left base. There were no mediastinal masses and no evidence of metastases, but scars in the right upper lobe suggested old tuberculosis. These findings, when compared with films taken

On the seventh hospital day an exploratory thoracotomy was performed.

DIFFERENTIAL DIAGNOSIS

DR. DONALD S. KING: We do not have the early x-ray films from the outside hospital, but I assume from the description that the fluid in the



FIGURE 1. Chest Plate Showing the Air Bubble in the Spherical Shadow in the Left Lower Chest

three days previously in another hospital, revealed no appreciable change.

The third day after admission a bronchoscopic examination was performed. The larynx, vocal cords and trachea were normal. The carina was sharp, and the right tracheobronchial tree normal. The left-upper-lobe orifice was normal, but approximately 1 cm. below it the lower-lobe bronchus was distinctly narrowed. The narrowing was due to constriction in size rather than to swelling of the mucosa. Because of this constriction only two or three terminals could be visualized. No neoplasm could be seen, and the orifices exuded no secretion.

left pleural cavity displaced the heart to the right, and that after the dry taps the fluid diminished greatly and the abnormal x-ray shadow was much smaller.

DR. AUBREY O. HAMPTON: These are the films taken at a later date in the outside hospital. Our films, taken two days later, show the same findings. The gas bubble within the hemispherical shadow described at the left base shows very plainly (Fig. 1). The shadow is quite sharp, and is continuous with the diaphragm and pleural surface. The second gas bubble described is not easy to see. It was thought that the second bubble was farther forward than the first.

DR. KING: I shall assume, then, that there were two bubbles, one anterior and well away from the hemispherical shadow described, and the other within the shadow itself. Am I correct in this, Dr. Hampton?

DR. HAMPTON: Yes. The thickness of the wall of this cavity, as demonstrated by the shifting of the gas bubble, is given as 10 to 4 mm. I should say that it was even thicker than 10 mm. at its greatest width. The fixation of the diaphragm was described, and one can see the splenic flexure and the gas bubble in the stomach. There is no hernia. There is density in the left lung, along the left border of the heart.

DR. KING: We have settled the problem of the two bubbles and have Dr. Hampton's description of the thickness of the wall of the cavity. There is also, I believe, evidence of pleural involvement.

DR. HAMPTON: Obviously, yes, and pleural fluid.

DR. KING: Outside the mass?

DR. HAMPTON: Yes.

DR. KING: The story is one of a man who eight weeks before admission, following an upper-respiratory infection, developed cough, purulent sputum, irregular fever, pleural pain and a weight loss of 20 pounds. Laboratory examination showed a high white-cell count, a high sedimentation rate, apparently no foul sputum and no tubercle bacilli. X-ray examination showed a sharply defined, hemispherical shadow, which apparently communicated with the bronchus because after postural drainage there was a definite change in the size of the bubble.

DR. HAMPTON: The bubble was not visible by fluoroscopic examination before postural drainage.

DR. KING: Could it be seen afterward?

DR. HAMPTON: Yes.

DR. KING: So you are willing to say there was communication with the bronchus in that area?

DR. HAMPTON: Yes.

DR. KING: There was, then, a cavity containing fluid and communicating with a bronchus, but besides this there must have been fluid in the pleural cavity itself. I cannot conceive of a cyst-like cavity large enough to give the shadow originally described and later shrinking to the size of the shadow now under discussion.

From the description of the first bronchoscopic examination I believe that a small but otherwise normal bronchus was seen. In the report of the one done in this hospital no mention is made of involvement of the mucosa, of tumor outcropping or of pressure from outside the bronchus. Did you bronchoscope him, Dr. Adams?

DR. RALPH ADAMS: Yes. When Dr. Chamber-

lain bronchosoped the patient outside the hospital, he found the same amount of narrowing as we found here and suggested verbally that edema might have been the cause of the narrowing. But when we bronchosoped him the extent of the narrowing was exactly the same, and there was no edema.

DR. KING: That sounds like an abnormally small bronchus. I cannot make anything else out of it.

It seems to me that there are six possible explanations for the picture as presented. The mass could be a malignant tumor with central necrosis; we have had cases of carcinoma in which the tumor has broken down, discharged into a bronchus and presented the x-ray picture of a shifting fluid level, but I cannot remember any case in which there has been such complete breaking down and such free bronchial drainage from the necrotic cavity. Secondly, we could be dealing with bronchiogenic carcinoma and a pulmonary abscess secondary to bronchial obstruction, but the x-ray appearance is not that of typical abscess and the patient is not so sick as is to be expected in such cases; the anterior bubble described could be a small pulmonary abscess, but I do not believe that it is. A benign bronchial tumor, perhaps an adenoma, with a secondary abscess is also a possibility. This seems to me unlikely because bronchial adenomas are almost always seen in the larger bronchi through the bronchoscope, and they usually give a history of gradually increasing cough and hemoptysis and not the onset described in this case. True pulmonary abscess without pre-existing bronchial obstruction — another possible explanation — at times gives clear-cut round shadows almost indistinguishable from tumors, and such an abscess could be accompanied by a pleural effusion; in this case, however, there has been no foul sputum, and a non-putrid abscess with this x-ray picture is certainly rare. The fifth possibility is encapsulated empyema. In my experience such an empyema is associated with a foul pleural fluid and has developed only after the rupture of a small subpleural abscess; there is no evidence in the record of such an abscess or such severe symptoms as usually follow an empyema of this sort. This brings me to the possibility of a cyst which has become secondarily infected. I do not know how to explain the picture on any other basis. If it is a cyst, it may be congenital or "secretory." In the first case there is an anatomic abnormality present from birth, and in the second interference with drainage of the secretions may come about after birth. We have had one case of an infected

congenital cyst that was very much like the present one. The patient was operated on once for empyema but was later shown to have a congenital cyst with a complete congenital stenosis of the bronchus leading to the posterior portion of the left lower lobe. In today's case I am assuming that the bronchoscopy did show an anatomic variation of the left-lower-lobe bronchus that was associated with the presence of a congenital cyst in the area beyond the reach of the bronchoscope. My diagnosis, then, is congenital cyst that has become secondarily infected and has led to a neighboring infection in the pleural space.

DR. TRACY B. MALLORY: Has anyone else a suggestion?

DR. EDWARD D. CHURCHILL: Why do you rule out empyema so lightly?

DR. KING: Because in my experience in cases like this there has always been a pre-existing pulmonary lesion that has led to a pleural fistula and empyema. Perhaps I should pay more attention to the possibility that an empyema ruptured into the bronchus from the outside.

DR. CHURCHILL: I find that a good many streptococcal empyemas develop bronchial fistulas.

DR. KING: Do they? Can a streptococcal empyema give this picture?

DR. CHURCHILL: I should think so.

DR. KING: Certainly the sharply defined shadow is not inconsistent with encapsulated pus.

DR. CHURCHILL: In referring to the description of the previous films, you said yourself that there was fluid in the pleural cavity.

DR. HAMPTON: Do you think the wall of this cavity is thicker than that of the congenital cyst you mentioned?

DR. KING: No. As I recollect the wall of the congenital cyst was quite thick in certain portions. Other types of cysts would have a thinner wall.

DR. CHURCHILL: I should say the walls of congenital cysts were very thin.

DR. MALLORY: I think that I should agree with Dr. Churchill. Anatomically they are thin. I do not know how they look by x-ray examination.

DR. KING: Look at this photograph of the proved congenital cyst.

DR. CHURCHILL: What is its thickness in millimeters, Dr. Hampton?

DR. HAMPTON: I have to admit that the wall is as thick as this one in some places, but very thin in others.

DR. KING: I grant you that, but I am sure that cysts proved at operation to be thin-walled have given the x-ray appearance of thick walls. Here is an example.

DR. MALLORY: We have to count on Dr. Adams to tell us most of the pathology because, thanks to him, the patient survived.

CLINICAL DIAGNOSIS

Carcinoma of the left lung?

DR. KING'S DIAGNOSIS

Congenital cyst of lung, with secondary infection.

ANATOMICAL DIAGNOSIS

Encapsulated empyema.

PATHOLOGICAL DISCUSSION

DR. ADAMS: Dr. Lowrey F. Davenport and I saw the patient together in consultation during the summer when our chiefs were away. The atypical pneumonia, the variability of the clinical symptoms, the evidence of pleural involvement, the suggestion of abscess as indicated by the fluid level and the evidence of bronchoscopy of narrowing of the lower lobe bronchus made us think that this was a case almost identical with one we had previously seen in which at operation there was a thick-walled peripheral abscess secondary to primary cancer of the bronchus. That was our pre-operative diagnosis.

At operation the pleura was found adherent laterally, as anticipated. It was edematous and thickened. When it was opened posteriorly the lower lobe was found collapsed, and where the incision was carried anteriorly, a circular abscess cavity was opened. It seemed that an ordinary encapsulated empyema had been entered. Dr. Benjamin Castleman was called, and a frozen section on a specimen from the abscess wall confirmed the presence of inflammatory tissue and the absence of malignant tissue. The patient made a rapid, uneventful recovery from this encapsulated empyema.

DR. KING: What was the organism?

DR. ADAMS: Both alpha and beta hemolytic streptococci were grown on culture.

DR. MALLORY: The biopsied specimen from the deep wall of the cavity showed an organizing pneumonitis underneath a lot of fibrous tissue and granulation tissue.

DR. ADAMS: This case was shown to several notable men in the thoracic field during the summer, and no one has yet made the correct diagnosis.

DR. KING: Dr. Churchill did.

DR. CHURCHILL: I merely raised the question.

DR. HAMPTON: He had no responsibility.

CASE 26452

PRESENTATION OF CASE

A thirty-year-old single woman entered the hospital complaining of shortness of breath and a chronic cough associated with sputum.

Because of the patient's poor condition the history was obtained from her sister. In another hospital, three years before admission, the patient had had a right radical mastectomy for carcinoma of the breast, followed by x-ray sterilization. Monthly x-ray examinations for the ensuing half year were negative. Two and a half years before admission the patient caught cold and developed a cough. Her physician said that she had "bubbles" in the chest, and although she continued to work for the next two weeks, the cold became much worse and she felt delirious and feverish. Her physician then made a diagnosis of pneumonia, and she remained in bed for the next month. After this illness she remained well until two years before entry, when she again caught cold, developed a cough with yellow sputum, a "rubbing" pain in the chest and a temperature of 103°F. She was treated with adrenalin, a cough medicine, codeine, a chest binder and sulfapyridine for the next month, but the cough persisted. Five months before admission she developed marked shortness of breath on exertion, was compelled to rest three or four times when climbing a flight of stairs and needed two pillows at night. She became easily fatigued and exhausted, and noticed "skipped" beats in the heart. A paroxysmal cough occasionally produced yellow sputum. An electrocardiographic recording three months before admission was normal, but an x-ray examination two months later revealed "fluid in the chest." On the same day a paroxysm of coughing produced blood-streaked sputum, and later the patient brought up a dark red clot. The next morning she entered another hospital, where a chest tap yielded one quart of lemon-colored fluid from the left side. This was repeated one week later, but "only a little blood" was obtained. Two and a half weeks before entry, sulfapyridine therapy was instituted, but discontinued because of nausea and vomiting. Five days later the patient was given sulfathiazole, which was continued for one week. Four days before entry she left the hospital and remained at home without medical care until the time of admission.

The family history and past illnesses were irrelevant.

Physical examination showed the patient to be dehydrated, toxic and acutely ill. The right breast had been amputated. The fingers were clubbed, and the nails showed an increased curvature. The

tongue was dry and coated. Examination of the heart was negative; the blood pressure was 120 systolic, 72 diastolic. The left chest was flat to percussion, with a point of maximum dullness at the angle of the scapula. Breath sounds were absent over the lower half of this side of the chest. The liver was palpable two fingerbreadths below the costal margin.

The temperature was 101.6°F., the pulse 126, and the respirations 28.

Examination of the urine showed a + test for albumin. No sputum could be obtained for examination. Examination of the blood showed a red-cell count of 2,920,000 with a hemoglobin of 78 gm. (photoelectric-cell technic), and a white-cell count of 9000. A blood Hinton test was negative.

X-ray examination of the chest showed a normal lung and diaphragm on the right side. The left side of the diaphragm—demonstrated by a gas bubble in the stomach, but not seen at its upper border—was slightly elevated. There was density in the entire area of the left lower lobe, which was homogeneous except in its central portion, where there was an irregular cavity. The cavity appeared to be near the center of the lobe. No fluid level was demonstrated.

An operation was performed on the second hospital day.

DIFFERENTIAL DIAGNOSIS

DR. EDWARD D. CHURCHILL: We have no x-ray report from six months after the cancer of the breast was removed to a date two months before admission—a period of two to three years.

As we read the story up to the physical examination I think that we are, of course, following the lead that is offered by the preceding history of cancer of the breast and thinking seriously of pulmonary metastases. The patient, when she entered the hospital, complained of chronic cough associated with sputum, but there is no note regarding the sputum, and, of course, we should be interested to know whether the sputum was purulent or bloody and what the microscopic examination showed.

What might this be? First of all, metastasis of cancer of the breast. Metastatic cancer of the lung rarely produces bloody sputum, or clubbing of the fingers unless a large bronchus is blocked. The strict localization of the disease to one region, with a clear opposite lung, is against metastases from a cancer of the breast. Dr. George W. Holmes's advice is always in my mind; namely, that a past history of cancer will lead one astray just as often as it will put one on the right track. I am therefore going to exclude a metastatic lesion from the breast from my list of preferred diag-

noses. However, we know that the behavior of cancer is unpredictable, and the tradition in these exercises is to fit everything together in one diagnosis.

This might be a primary tumor of the lung. The past history of cancer probably makes it even more likely that this patient would have a primary tumor of the lung than would a random representative of the general population. The history is consistent with a primary lesion of the lung. We may cheat a bit and say that the surgeon in charge probably would have bronchoscoped the patient instead of operating if he had thought that it was a primary tumor of the lung—but he might not have arrived at the correct diagnosis himself.

I am afraid that for practical purposes I have to come down to a diagnosis of empyema. I do not know when it started. It might have started with the second attack of pneumonia—when the patient had the “rubbing” pain in the chest. We have in the record a history of fluid that was aspirated and described as lemon-colored—a quart of it. That might have gone on and thickened to form the empyema, or there might have been a separate pocket of localized empyema that was never reached by any tap. The basal situation of this lesion suggests the so-called “intrapneumonic type” of empyema that lies between the lower lobe and the diaphragm. The clubbing of the fingers does not usually occur with encapsulated empyema unless a bronchial fistula develops, and then we commonly see pulmonary osteoarthropathy. If a patient has an empyema and has been coughing and raising yellow sputum, it is fair to assume that a bronchial fistula and clubbing of the fingers might follow. The absent breath sounds are not typical of empyema. We should expect a diminished bronchial breathing. However, with marked fixation of the diaphragm and a splinting of the chest wall, bronchial breathing may often be so distant that it is described as absent. There was probably some diminished excursion of the chest, as indicated by a narrowing of the intercostal spaces. If we had been privileged to examine the patient at the time this x-ray film was taken, we should have observed that she was not moving the lower portion of the left chest. That again indicates pleural involvement and pleural infection. Against the hypothesis of an empyema is the position of the shadow, which is described as being near the center of the lobe. Dr Hampton, this is not a true lateral film, but as you can see, is somewhat oblique, throwing the left side quite a bit forward. Might not the cavity be peripheral?

DR AUBREY O HAMPTON: That is a portable film and the apparent rotation is due to magnification. I should not think it is as much rotated as you at first thought. One must localize the cavity in a position away from the chest wall.

DR CHURCHILL: And deep within the chest? Whether it is within the lobe is another thing. They went too far with that, did they not?

DR HAMPTON: It is in the lower lobe.

DR CHURCHILL: It appears to occupy the region where the lobe commonly lies.

DR HAMPTON: That is a more accurate statement.

DR CHURCHILL: I am going to make a diagnosis of encapsulated empyema with a bronchial fistula.

DR HAMPTON: Complete consolidation in the left lower lobe gives a picture exactly like fluid—the same shape and everything.

DR DONALD S KING: But not displaced mediastinum.

DR HAMPTON: The patient has scoliosis. Perhaps she had it before this illness.

DR CHURCHILL: I shall make a diagnosis of encapsulated empyema.

Without hedging I want to call attention to something I think we have perhaps forgotten in this case, and certainly in the case Dr King discussed—it is an old trick that the late Dr William H. Smith taught me in examining the sputum in a case of long standing encapsulated empyema draining into a bronchus. He always maintained that a pocket of pus in the pleura will for a long period retain its bacteriological purity. In the case Dr King discussed, examination of the sputum, if it had been done by smear and gram stain, might have revealed a clear-cut predominance of chains of streptococci. Of course we should like that type of information in this case. The empyema may have been due to a streptococcus or to some other organism, but it is the predominance of any one organism in the smear of the sputum that may give you the lead.

DR TRACY B MALLORY: Perhaps Dr Davenport can give us more exact information.

DR LOWREY F DAVENPORT: The patient was coughing but not raising anything, and consequently had no sputum to be examined at the time she came in. When we tapped the posterior chest below the angle of the scapula and obtained frank pus we reasoned about the case as Dr Churchill has. By tying together the previous history of pneumonia, the lemon-colored fluid and the finding of pneumococci in the pus, we thought we were safe in assuming that this was an encapsulated pneumococcal empyema. It was with that

diagnosis that the patient was transferred for rib resection.

DR. CHURCHILL: How much pus did you obtain from the chest tap? Was it a free flow or a very small amount?

DR. DAVENPORT: I recall that about 60 cc. of frank pus was removed.

DR. CHURCHILL: Of course, one can get a small amount of pus from tapping a drowned lung, but with the added information of 60 cc. of freely flowing pus, I should certainly be on the side of the surgeon who operated with the diagnosis of encapsulated empyema.

DR. KING: That seems easy.

DR. RALPH ADAMS: Do you mean that you agree, Dr. King?

DR. KING: I do not see how I can make any other diagnosis.

DR. HAMPTON: How do you explain the fact that the cavity was in the center of the lobe, away from the chest wall and near the center of the dense shadow?

DR. KING: It remains to be proved that it was in the lung.

DR. DAVENPORT: In doing the chest tap I believed that I was going through a very thick pleura.

DR. ADAMS: The diagnosis of encapsulated empyema was apparently confirmed at operation, and thick pus, in addition to what Dr. Davenport removed, was evacuated. The pleura was greatly thickened. In the base of the empyema cavity the tissue was irregular and necrotic, somewhat different from that which lined the remainder of the cavity. We did not know how to interpret it, and we therefore put a tube into the cavity, as is usually done for such cases. The following morning the patient began to lose air through the tube, which was indicative of a bronchial fistula. That did not occur until twelve hours after the operation. Still later, she began to cough up some blood, and the temperature rose rapidly. She died the following day.

DR. MALLORY: Is there anything of interest in the post-mortem films?

DR. HAMPTON: I should like to show that Dr. Adams put the tube directly into the cavity that the films had demonstrated.

CLINICAL DIAGNOSIS

Encapsulated empyema.

DR. CHURCHILL'S DIAGNOSIS

Encapsulated empyema, with bronchial fistula.

ANATOMICAL DIAGNOSES

Carcinoma, metastatic, of bronchus, lung, bronchial lymph nodes, mediastinum and pleura.
Lobar pneumonia, Type 3 pneumococcus, left lower lobe, unresolved.

Lung abscess, acute, left lower lobe.

Pleuritis, chronic fibrous and acute fibrinous, left.

Pulmonary edema, slight, right lower lobe.

Arteriosclerosis, moderate, coronary.

Operative scar: right radical mastectomy; left thoracotomy.

Osteoarthritis of fingers.

PATHOLOGICAL DISCUSSION

DR. MALLORY: At autopsy it was apparent that all the pathologic lesions had not been revealed at operation. We could identify no empyema cavity. The lower lobe on the left felt solid on external palpation, but on cutting into it a large central abscess cavity was found, nearly 4 cm. in diameter. Dr. Adams's drainage tube lay in this cavity, the walls of which varied in consistence. The lower and lateral portions were somewhat soft but tough, and evidently consisted of organized lung tissue—an organizing pneumonitis. On the upper and medial surfaces the walls were relatively hard, and it was at once apparent that this was metastatic tumor. The carcinomatous mass involved chiefly the apex of the lower lobe, surrounding all the bronchi and markedly narrowing the lumens, without invading any bronchus, however. There were three bronchi that communicated with the abscess cavity. The tumor had also extended into the mediastinal nodes, where a large mass of tumor tissue was also found. We did not find any other spots of metastatic tumor in the post-mortem examination, in either the upper lobe or the opposite lung. The abscess fluid at autopsy was not foul, and the process was apparently still a pure pneumococcal infection.

DR. CHURCHILL: Did the cancer cause the empyema, or was it an incidental finding?

DR. MALLORY: It had certainly caused bronchial stenosis, and I think it is fair to assume with infection of the lung that the stenosis might have prevented normal resolution of a coincidental pneumococcal pneumonia.

DR. HAMPTON: How many lung abscesses have you seen due to metastatic cancer?

DR. MALLORY: Offhand I do not remember any other. It very commonly results from bronchiogenic carcinoma, of course.

The New England Journal of Medicine

Formerly the
Boston Medical and Surgical Journal
Established in 1823

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE
ON PUBLICATIONS

Official Organ of

THE MASSACHUSETTS MEDICAL SOCIETY
THE NEW HAMPSHIRE MEDICAL SOCIETY
THE VERMONT STATE MEDICAL SOCIETY

EDITORIAL BOARD

Joseph Garland M D	John P. Sutherland M D
William B. Breed M D	Stephen Rushmore M D
George R. M. not M D	Henry R. Vets M D
Frank H. Lahey M D	Robert M. Green M D
Sheldr Warren M D	Charles C. Lund M D
George L. Tobey Jr M D	John F. Fulon M D
C. Guy Lane M D	A. Warren Searles M D
William A. Rogers M D	Dwight O'Hara M D

ASSOCIATE EDITORS

Thomas H. Lanman M D	Donald Munro M D
Henry Jackson Jr M D	
Walter P. Bowers M D	EDITOR EMERITUS
Robert N. Nye M D	MANAGING EDITOR
Clara D. Davis	ASSISTANT EDITOR

SUBSCRIPTION TERMS \$6.00 per year in advance postage paid for the
United States Canada \$7.04 per year \$8.52 per year for all foreign coun-
tries belonging to the Postal Union

MATERIAL for early publication should be received not later than noon
on Saturday

THE JOURNAL does not hold itself responsible for statements made by any
contributor

COMMUNICATIONS should be addressed to the *New England Journal of
Medicine* 8 Fenway Boston Massachusetts

an extraordinary demonstration of the will to learn on the part of the medical profession at large may well be regarded as indisputable evidence that the health problems of the western three quarters of North America are in good hands and that the community at large need have no fear for its well being. It is perhaps not saying too much to state also that this meeting is evidence of a type of altruistic humanism and humanitarianism that will in the end serve to lead the world out of its present chaotic barbarianism.

Next week, New England has her third post-graduate assembly, modeled on the larger organization but cut down to fit a smaller territory and fewer doctors. Every registered physician in this area has been invited to attend. The appeal is universal rather than specialized, and the conduct of the meeting may be expected to reach the high efficiency of its predecessors. There can be no question of the will to learn on the part of the local profession, therefore, let them compliment the speakers, evidence their faith in the managing committee and profit their own interests by attending in even larger numbers than they have in the past two years.

THE WILL TO LEARN

THREE weeks ago the Interstate Postgraduate Medical Association of North America held its five-day annual meeting at Cleveland. The public auditorium, an enormous hall with a seating capacity of thousands, was hired for the purposes of the daily assembly and the housing of the commercial and scientific exhibits. Five thousand physicians were registered. The majority came from the Midwest but many were from communities as distant as Texas, California and Canada. They met every morning at eight o'clock, and adjourned at nine or ten o'clock at night, having had an hour's respite for both lunch and dinner. Every paper and presentation was started and stopped on the minute. The program was general and had a wide medical appeal. The association first met in a small church a number of years ago and has steadily grown, until last year at the Chicago meeting the attendance was six thousand. Such

THE COURT OF LAST APPEAL

THE comparative value of different methods for the demonstration of tubercle bacilli has been well shown by Pinner and Wooley¹ in their study of 239 specimens of sputum from tuberculous patients, all of which were reported "negative on direct smear." Further search for tubercle bacilli in these same specimens by other methods revealed that no less than 10 per cent were positive by the sputum concentration technique, 56 per cent by culture, and 77 per cent by guinea pig inoculation. These figures show clearly that the unqualified term "negative sputum" is practically meaningless.

The absence of sputum in children led to the study of the gastric contents as a source of tubercle bacilli. Meunier in 1898 opened the way for this method in the diagnosis of tuberculous pulmonary lesions. Since then, aspiration of the fasting stomach contents has become well established as a noteworthy procedure for the di-

agnosis of primary and reinfection types of tuberculosis in infants and children. Recently this technique has been applied to adults. Sweany and his co-workers² believe that it is better than any other method in establishing active tuberculous foci. They further state that "no patient with clinical signs of tuberculosis who has negative sputum should be considered negative for the disease until stomach lavage has yielded negative results."

Stiehm³ has presented an excellent study of 70 cases of subclinical tuberculosis that presented x-ray evidence of small pulmonary infiltrations. Usually there was no expectoration, and sputum, when present, was negative in every case by direct smear. As Pinner and Wooley concluded from their figures for sputum, Stiehm found that injection of the fasting gastric contents into guinea pigs was the most reliable method of proving the activity of these small lesions. The repeated presence of tubercle bacilli in the gastric contents of the subclinical cases usually indicated an unfavorable course, whereas their repeated absence gave almost complete assurance of a favorable outcome. A change of the gastric contents from positive to negative was a favorable prognostic sign. He found that sedimentation rates, white-cell counts and differential counts were significantly unreliable signs in these early cases.

Stiehm's method for examining the gastric contents of adults consists in the aspiration of fasting specimens on three successive mornings, by means of a catheter passed through the nose. Ten to 15 cc. of stomach contents is usually withdrawn, but if nothing is obtained 15 cc. of sterile physiological salt solution is injected into the stomach and withdrawn fifteen minutes later. Following centrifugation, the sediment is examined by direct smear and is injected into a guinea pig in each case. In Stiehm's series of 40 cases with questionable lesions and "negative" or absent sputums, direct smears of sediments from the gastric contents were positive in 18 per cent, whereas guinea-pig inoculations were positive in 72 per cent.

These figures are worthy of respect and deserve

more widespread application. They point to a simple procedure that appears to contribute enormously not only to the accuracy of diagnosis in early tuberculosis but also to the means of determining the activity of minimal and subclinical lesions. Gastric lavage, when properly performed, is a procedure that may well be termed the "court of last appeal" in the search for tubercle bacilli.

REFERENCES

1. Pinner, M., and Wooley, M. T.: Negative sputum. *J. Thoracic Surg.* 5:476-480, 1936.
2. Stadnichenko, A.; Cohen, S. J., and Sweany, H. C.: Stomach lavage in the diagnosis and control of treatment of tuberculosis. *J. A.M.A.* 114:634-639, 1940.
3. Stiehm, R. H.: Subclinical pulmonary tuberculosis: a presentation of forty cases. *Ann. Int. Med.* 13:2285-2305, 1940. Tubercle bacilli in the gastric contents: an important diagnostic and prognostic finding. *Am. J. M. Sc.* 194:340-344, 1937.

MEDICAL EPONYM

ESMARCH BANDAGE

Johann Friedrich August von Esmarch (1823-1908), professor of surgery at Kiel, published a little booklet *Der erste Verband auf dem Schlachtfelde* [The First Bandage for Use on the Battlefield] (Kiel: Schwers'sche Buchhandlung, 1869). A sample of the bandage was pasted in the back of the book. The following translated description appears on page 9:

A three-cornered cloth of suitable size would be the best material for use as the first bandage on the battlefield. . . .

If one were to choose for the preparation of these cloths a very light-weight cotton shirting, one yard in width, and, if they were manufactured in large quantities, each one would cost only a few cents.

Such a cloth can be folded to the size of a playing card, and when pinned together with two or three large pins,—perhaps two inches long,—is about half an inch thick and weighs hardly an ounce, at any rate less than the bandage now carried by the soldier in his haversack.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

NEW ENGLAND POSTGRADUATE ASSEMBLY

The third New England Postgraduate Assembly will be held on November 13 and 14 at Sanders Theatre, Harvard University, Cambridge. Buffet luncheons will be served in Memorial Hall on both days. The dinner on Wednesday evening will be followed by a talk by Dr. Harrison S. Martland, of Newark, New Jersey, his subject being "Dr. Watson and Mr. Sherlock Holmes." The registration fee (\$3.00) does not include admission to the luncheons (75 cents) or the dinner (\$1.25). Those desiring luncheon or dinner

Tickets should apply immediately, if they have not already done so, to the Postgraduate Assembly Committee, 8 Fenway, Boston. Such applications should be accompanied by a check or money order, and if they are received by the committee during the week of the assembly, the applicant must claim his badge and tickets at the registration desk.

SECTION OF OBSTETRICS AND GYNECOLOGY*

RAYMOND S. TITUS, M.D., *Secretary*
330 Dartmouth Street
Boston

DIABETIC COMA ASSOCIATED WITH DELIVERY

Mrs. F. G., a nineteen-year-old primipara, known to have had diabetes for eleven years, was first seen with acute pyelitis on July 24, 1932, when six and a half months pregnant.

The family history was noncontributory. The patient's past history was irrelevant except for the diabetes. She had a diabetic retinitis. Catamenia began at twelve, were regular with a twenty-eight-day cycle, and lasted five days. The last period began on January 14, making her expected date of confinement October 21 to 27.

Physical examination showed a very well-developed young woman. The heart was not enlarged; there were no murmurs. The lungs were clear and resonant; there were no rales. The blood pressure was 122 systolic, 60 diastolic. Examination of the extremities was negative. The uterus was enlarged to a size corresponding to a pregnancy of twenty-six to twenty-seven weeks. There was tenderness in the region of the right costo-vertebral angle, and the urine was full of pus. Temperature had been ranging from 99 to 104°F. A diagnosis of pyelitis was made, but under conservative treatment it cleared up; the patient went on to term without an exacerbation.

On October 1 she was sent to the hospital. The weight was 136 pounds. The blood pressure was 110 systolic. Examination of the urine showed a slight trace of albumin, but there was no edema. The diabetes was well controlled. The uterus was big, and the fetal heart was audible. Vaginal examination showed the tissues to be soft, the cervix not obliterated and not open. The patient remained in the hospital until she started in spontaneous labor.

On October 8 vaginal examination was performed. The cervix was very soft and dilated to admit one finger, but the canal was rather long. It was planned to induce labor in another week.

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

On October 13 she started in labor. Examination at 8:30 a.m. revealed a very soft cervix, dilated to admit two fingers but not flat. The membranes were ruptured, and 2 minims of posterior pituitary extract was given. At 10:00 a.m. the patient became unconscious. A specialist in diabetes was immediately summoned, and intensive treatment for the coma was instituted. At this time several examiners heard the fetal heart. A note says that at 9:00 p.m., when the cervix was dilated to admit four to five fingers, with the head well engaged, the fetal heart was audible. At 10:00 p.m. on October 13, after full dilatation, a baby weighing 9 pounds, 6 ounces, with beginning maceration, was delivered by a single forceps operation. Between noon on October 13, just after the patient went into coma, and noon on October 14, 300 units of insulin was given.

The convalescence was normal and satisfactory except for an attack of pyelitis that cleared up very quickly.

Comment. This case illustrates many things. In the first place this young woman was what is called an "insulin" diabetic patient. Diabetes developed at the age of eight years, and the patient would not have lived to reach maturity and to become pregnant had it not been for insulin.

This patient was hospitalized two weeks before spontaneous labor occurred at approximately thirty-eight weeks, and although she was under adequate treatment, coma developed shortly after the onset of labor. A specialist in diabetes, had one been in attendance, might well have appreciated the onset of coma. This emphasizes the need for having such a specialist present during all diabetic labors so that blood sugar tests may be done frequently, and impending coma diagnosed in time to prevent actual unconsciousness.

This case illustrates the danger of allowing patients with severe diabetes to go to spontaneous labor after viability. A cesarean section done any time before labor started would have produced a live child—one that in all probability would have survived. This case also illustrates the size of babies born of diabetic mothers and also how quickly maceration can occur. It is possible that the fetal heart was not heard at 9:00 p.m., but it is a fact observed by several different people that the fetal heart was audible at 10:00 a.m.

In a subsequent pregnancy this patient was aborted.

Until diabetes in pregnancy can be controlled better than it is at present, any patient with severe diabetes who goes beyond thirty-seven weeks with a viable child stands a definite chance of losing the fetus by intrauterine death unless labor is induced or a cesarean section performed.

MEDICAL POSTGRADUATE EXTENSION COURSES

The following sessions, given by the Massachusetts Medical Society in co-operation with the Massachusetts Department of Public Health, the United States Public Health Service and the Federal Children's Bureau, have been arranged for the week beginning November 11:

BARNSTABLE

Sunday, November 17, at 4:00 p.m., at the Cape Cod Hospital, Hyannis. Pediatric Case Discussions. Instructor: Louis K. Diamond. Donald E. Higgins, *Chairman*.

BRISTOL NORTH

Friday, November 15, at 4:00 p.m., at the Morton Hospital, Taunton. Acute Abdominal Pain: Its interpretation and management. Instructor: Richard B. Cattell. Lester E. Butler, *Chairman*.

BRISTOL SOUTH (New Bedford Section)

Friday, November 15, at 4:00 p.m., at St. Luke's Hospital, New Bedford. The Treatment of Varicose Veins. Instructor: Robert R. Linton. Robert H. Goodwin, *Chairman*.

ESSEX NORTH

Friday, November 15, at 4:30 p.m., at the Clover Hill Hospital, Lawrence. Obstetrical Complications with Case Histories and Clinical Problems. Instructor: Judson A. Smith. John Parr, *Chairman*.

ESSEX SOUTH

Tuesday, November 12, at 4:00 p.m., in the Conference Room, Salem Hospital, Salem. Nutritional Deficiencies and the Uses of Preparations of Vitamins. Instructor: Maurice B. Strauss. J. Robert Shaughnessy, *Chairman*.

MIDDLESEX NORTH

Friday, November 15, at 5:00 p.m., at St. John's Hospital, Lowell. Recent Advances in Medical Therapeutics. Instructor: Charles L. Short. William S. Lawler, *Chairman*.

PLYMOUTH

Tuesday, November 12, at 4:30 p.m., in the Nurses' Home of the Brockton Hospital, Brockton. Pediatric Case Discussions. Instructor: Lewis W. Hill. Walter H. Pulsifer, *Chairman*.

COMMITTEE ON INDUSTRIAL HEALTH

EXPLOSION HAZARDS IN STORAGE-BATTERY ROOMS

The results of a study of explosion hazards in storage-battery rooms are given in a report just issued by the Bureau of Mines, United States Department of the Interior. The study grew out of a co-operative investigation between the Bureau of Mines, the Boston Edison Company and the Boston Consolidated Gas Company which has been in force for a number of years and has been carried out primarily for the purpose of determining the explosion hazards in manholes, conduits and other unventilated spaces underground. Surveys were made in connection with this investigation to determine and eliminate the hazards due to hydrogen in the many large standby-type storage-battery rooms of one of the co-operative companies.

This report gives the average and maximum concen-

trations of hydrogen present in twenty-three battery rooms when the batteries were being charged and when the batteries were idle ("on float"). The battery rooms were all comparatively large, the volume of free air space in the rooms ranging from 13,445 to 86,678 cubic feet, and the number of cells in each installation varying from 82 to 344. Two or more surveys were made in each battery room during the investigation, covering a period of about four years. Approximately 5000 samples of battery-room atmospheres were taken and analyzed.

The investigation showed that the concentration of hydrogen in battery rooms was low and that no hazards were involved when the batteries were idle. Under this condition, the concentrations of hydrogen varied from zero to a maximum of 0.29 per cent. The only cases where hazardous concentrations of hydrogen were present were during the periods when the batteries were being charged and more especially toward the end of the charging period. The highest average concentration of hydrogen in any battery room tested was 5.35 per cent and was in the explosive range of hydrogen-air mixtures.

The results showed rather definitely that mechanical ventilation is the more satisfactory method of ventilation because the concentration of the hydrogen in the rooms ventilated by natural means averaged 50 per cent higher than that in rooms provided with mechanical ventilation. The charging rate was purposely changed during many of the surveys, and these results showed that in general the average hydrogen concentration found in the rooms was approximately proportional to the charging rate.

Although the information given in the report applies to certain battery rooms of one company, specific information relative to the details of the battery rooms, the cells and the ventilation equipment is given so that the results may be applied to various spaces in which hydrogen is liberated by electrolytic processes.

This report, described as Bureau of Mines Technical Paper No. 612, "Explosion Hazards in Storage Battery Rooms," by G. W. Jones, John Campbell, R. E. Dillon and O. B. Benson, may be purchased from the Superintendent of Documents, Government Printing Office, Washington, D. C., at a price of 10 cents.

DEATHS

CARLETON — RALPH CARLETON, M.D., of Springfield, died October 26. He was in his seventy-first year.

Born in Norwich, Connecticut, he received his degree from the Harvard Medical School in 1894. He served as an intern at the Carney Hospital and the Massachusetts Eye and Ear Infirmary in Boston before starting private practice in Springfield. Dr. Carleton was on the staff of the Springfield Hospital and was a fellow of the Massachusetts Medical Society and the American Medical Association. He held memberships in the American Academy of Ophthalmology and Oto-Laryngology, the New England Ophthalmological Society, the Springfield Academy of Medicine and the Springfield Medical Club.

His widow survives him.

HILL — GEORGE J. HILL, M.D., of Boston, died October 29. He was in his sixty-second year.

Born in Beverly, he attended Noble and Greenough School and received his degree from the Harvard Medical School in 1903. He also studied at the University of Berlin. Dr. Hill was then surgeon for the United Shoe Machinery Corporation in Beverly for fifteen years. In 1918, he moved to Boston, where he was a pediatrician on the

staff of the Children's Hospital

Dr Hill was a member of the Massachusetts Medical Society and the American Medical Association

His widow, a brother, two sons, a daughter and four grandchildren survive him

NOWELL—**HOWARD W NOWELL, M.D.**, of Brookline, died October 28. He was in his sixty ninth year.

Born in Merrimacport, he attended Lyndon College and received his degree from Boston University School of Medicine in 1911. He was a former pathologist at the Massachusetts Homeopathic Hospital and was instructor in pathology from 1911 to 1913 and then associate professor of pathology from 1913 to 1915 at Boston University School of Medicine. Dr. Nowell was a fellow of the Massachusetts Medical Society and the American Medical Association.

His widow survives him.

PARKER—**RAYMOND B PARKER, M.D.**, of Winthrop, died October 19. He was in his fifty sixth year.

Dr Parker was born at Reading and attended Dartmouth College, receiving his degree from Harvard Medical School in 1912. He interned at the Boston City and Boston Lying in hospitals, and was later house physician at the Boston Lying in Hospital. From 1914 to 1915 he was instructor in obstetrics at the Harvard Medical School. A former chairman of the Winthrop Board of Health, he was also school physician there for twenty years.

Dr Parker was a fellow of the Massachusetts Medical Society and the American Medical Association.

His widow, his mother, a daughter, a son and a sister survive him.

MISCELLANY

NATIONAL HEALTH LIBRARY

The National Health Library, which completed two decades of service this year, announces its removal from the RCA Building in Rockefeller Center to 1790 Broadway, New York City. Since its establishment twenty years ago, this library has brought together one of the best collections of source material in the United States on public health, sanitation, health education and related subjects. It includes 6000 volumes and 30,000 pamphlets. More than 500 medical and public health periodicals are received regularly from all parts of the world.

Administered by the National Health Council, the library is intended primarily for the use of the seventeen health organizations that are members of the council. Persons who are not members of the supporting organizations may have the privilege of using the library by paying a small annual fee.

Members from all over the country avail themselves of the privilege of borrowing books from the library. Nurses and public health workers in small towns in which there are no libraries are especially grateful for the service. Material may be found in the National Health Library that might take days and even weeks to unearth elsewhere. The indexing of this material makes it of especial value for research workers.

To make the current material useful, all periodicals are indexed in a card catalog. Every week a mimeographed list of the more important articles is issued under the title, *The Library Index. A weekly index to current periodical literature in the field of public health.* This publication is available to the public for a small annual subscription.

The National Health Council includes the following active member agencies: American Society for the Hard of Hearing, American Heart Association, American Public Health Association, American Red Cross, American Social Hygiene Association, American Society for the Control of Cancer, Conference of State and Provincial Health Authorities of North America, Maternity Center Association, National Committee of Health Council Executives, National Committee for Mental Hygiene, National Organization for Public Health Nursing, National Society for the Prevention of Blindness and the National Tuberculosis Association. The United States Children's Bureau and the United States Public Health Service are advisory members of the council. The American Nurses' Association and the Foundation for Positive Health are associate members.

VITAMIN FREE FOODS

A recent announcement by the research laboratories of the S M A Corporation reveals that they are now in a position to provide vitamin free casein and other vitamin free foods to research workers who have previously been obliged to manufacture these items.

For many years the company's research laboratories have been producing these foods exclusively for their own use. With expansion of their facilities they are now able to provide vitamin free foods to others at an exceptionally reasonable cost, and this should prove to be a great convenience to those who are engaged in this type of investigative work. Quantities of 1, 5, 10 or 100 pounds, or even more, may be ordered directly from the Research Laboratories, S M A Corporation, Chagrin Falls, Ohio.

NOTES

Twenty four appointments to the teaching and research staff of the Harvard Medical School were recently announced by the University as follows (effective September 1, 1940): Edward A. Gall, M.D. Tulane '31, instructor in pathology; Thomas H. Weller, M.D. Harvard '40, teaching fellow in bacteriology; Kirk T. Mosley, M.P.H. Harvard '40, assistant in epidemiology; Joseph R. Frothingham, M.D. Harvard '37, assistant in medicine; Herbert I. Harris, M.D. Tufts '36, assistant in neurology; Earl S. Seale, M.D. Tulane '35, assistant in ophthalmology; Vincent G. Ryan, M.D. Yale '34, assistant in psychiatry; Elvin V. Semrad, M.D. University of Nebraska '34, assistant in psychiatry; Howard A. Bouve, M.D. Harvard '21, assistant in surgery; Lee G. Kendall, M.D. Harvard '30, assistant in surgery; Howard Ulfelder, M.D. Harvard '36, assistant in surgery; Alfred L. Florman, M.D. Johns Hopkins '38, research fellow in bacteriology; David E. Green, Ph.D. University of Cambridge, England, '34, research fellow in biological chemistry; Laurence L. Strong, Ph.D. Brown University '40, research fellow in physical chemistry; Isadore Fankuchen, Ph.D. Cornell '33, research fellow in physical chemistry; Carl C. Jensen, S.M. University of Nebraska '29, research fellow in physical chemistry; Donald Murnaghan, M.B., B.Ch., B.A.O., National University of Ireland '37, research fellow in medicine; George E. Hobbs, M.D. University of Toronto '33, research fellow in neurology; Charles C. Roby, Ph.D. University of Chicago '40, research fellow in obstetrics; Oliver H. Straus, M.D. Columbia '40, research fellow in pharmacology; Effren C. Del Pozo, M.D. National University of Mexico '36, research fellow in physiology; Harold I. Harvey, M.D. Duke University '37, research fellow in psychiatry, (effective November 1, 1940); Charles R. Harrison, Ph.D. University of Illinois '40, research fellow in physical chemistry.

istry; (effective January 1, 1941) Edwin L. Cantlon, M.D. Harvard '36, assistant in surgery.

Harvard University has recently announced the promotion of Dr. John E. Gordon, professor of preventive medicine and epidemiology at Harvard Medical School and director of the new Harvard Public Health Unit and Harvard-Red Cross Hospital Unit in England, to Charles Wilder Professor of Preventive Medicine and Epidemiology. This professorship, held by Dr. Hans Zinsser as head of the Department of Bacteriology and Immunology from 1935 until the time of his death this fall, now returns to the department to which it was originally allocated, Dr. Milton J. Rosenau, of the Department of Preventive Medicine and Epidemiology, having been the holder of the chair from its founding in 1909 until his retirement in 1935.

CORRESPONDENCE

ARMY MEDICAL LIBRARY

To the Editor: I am directed by the Surgeon General to inform you that authors' reprints are gratefully received at the Army Medical Library. They are placed in a special collection catalogued by author and thus form a ready bibliography of the work of any given writer and a valuable supplementary source of material when the volume of original publication is temporarily unavailable at the bindery or on loan.

HAROLD W. JONES, *Librarian*,
Colonel, Medical Corps, United States Army.

ARTICLES ACCEPTED BY THE AMERICAN MEDICAL ASSOCIATION, COUNCIL ON PHARMACY AND CHEMISTRY

To the Editor: In addition to the articles enumerated in our letter of September 4 the following have been accepted:

Abbott Laboratories

- Bismo-Cymol 60-cc. bottle
- Bismo-Cymol 500-cc. bottle
- Ampoules Procaine Hydrochloride, 1 per cent, W/V, 1.5 cc.
- Ampoules Procaine Hydrochloride, 1 per cent, — Epinephrine 1:50,000 Solution, 2 cc.
- Butyn Sulfate Tablets, 25 mg.

Cheplin Biological Laboratories

- Cheplin's Solution of Sodium Cacodylate with Benzyl Alcohol:
 - 0.05 gm. ($\frac{3}{4}$ gr.), 30-cc. vial;
 - 0.2 gm. (3 gr.), 30-cc vial;
 - 0.3 gm. (5 gr.), 30-cc. vial;
 - 0.5 gm. ($7\frac{1}{2}$ gr.), 30-cc. vial;
 - 0.065 gm. (1 gr.), 1 cc.

Endo Products, Incorporated

- Ampoules Mercury Succinimide, 0.01 gm. ($\frac{1}{8}$ gr.), 1 cc.
- Ampoules Sodium Thiosulfate Solution, 0.5 gm. in 5 cc.
- Ampoules Sodium Thiosulfate Solution, 1.0 gm. in 10 cc.
- Tablets Sulfanilamide—Endo, 5 gr.
- Tablets Sulfanilamide—Endo $7\frac{1}{2}$ gr.

The National Drug Co.

- Parenteral Solution of Liver, 10-cc. ampul vials, 5 U.S.P. injectable units per cc.

Parenteral Solution of Liver, 10-cc. ampul vials, 10 U.S.P. injectable units per cc.

Parke, Davis and Company

- Capsules Sulfapyridine, 0.25 gm. ($3\frac{3}{4}$ gr.)

Riedel-de Haen, Incorporated

Pernoston Sodium

- Ampules Pernoston Sodium, 10 per cent. 2 cc.

Smith-Dorsey Company

- Phenobarbital Tablets, 0.1 gm. ($1\frac{1}{2}$ gr.)
- Tablets Aminophyllin, 0.1 gm. ($1\frac{1}{2}$ gr.)

Frederick Stearns and Company

- Tablets Thiamine Hydrochloride, 5 mg.
- Tablets Thiamine Hydrochloride, 10 mg.

E. R. Squibb and Sons

- Solution Thiamine Chloride—Squibb, 5-cc. vial, 100 mg. per cc.

Upjohn Company

- Hypodermic Tablets Procaine Hydrochloride, 0.65 gm.
- Hypodermic Tablets Procaine Hydrochloride, 0.12 gm.
- ($\frac{1}{2}$ gr.), with Epinephrine, 0.025 mg. (1/2500 gr.)

PAUL NICHOLAS LEECH, *Secretary*

535 North Dearborn Street,
Chicago, Illinois.

NOTICES

PETER BENT BRIGHAM HOSPITAL

A joint medical and surgical clinic at the Peter Bent Brigham Hospital will be held on Wednesday, November 13, from 2:00 to 4:00 p.m. Drs. Edward S. Emery and Robert Zollinger will speak, their subject being "Diarhea and Constipation." A clinicopathological conference, conducted by Dr. Elliott C. Cutler, will take place from 4:00 to 5:00 p.m.

Physicians and students are cordially invited to attend

BOSTON GASTRO-ENTEROLOGICAL SOCIETY

The next meeting of the Boston Gastro-Enterological Society will be held in the Carney Hospital Auditorium on Wednesday, November 13, at 12:00 m.

PROGRAM

- Necessity of Surgical Intervention in Intractable Peptic Ulcers. Dr. William E. Browne. Discussed by Dr. Norman A. Welch.
- Physiological Rest in the Treatment of Diabetes. Dr. Charles W. Finnerty. Discussed by Dr. G. Herbert Cleary.
- Gastrointestinal Symptoms in Urologic Disease. Dr. Francis J. West. Discussed by Dr. C. J. E. Kichham.

BOSTON ORTHOPEDIC CLUB

The next meeting of the Boston Orthopedic Club will be held in Ware Hall, Boston Medical Library, 8 Fenway, Boston, on Monday, November 18, at 8:00 p.m. Dr. Fritz Teal, of Lincoln, Nebraska, will speak on "The Orr Treatment of Compound Fractures."

Regular monthly meetings of the Boston Orthopedic Club will be held on the third Monday of every month until May 19.

GREATER BOSTON MEDICAL SOCIETY

There will be a meeting of the Greater Boston Medical Society in the auditorium of the Beth Israel Hospital on Tuesday, November 12, at 8:15 p.m. Dr. Austin M. Brues will speak on "Recent Advances in the Study of Cancer." Mrs. Harry F. Friedman and Waldo E. Cohn will discuss the subject.

CARNEY HOSPITAL

The monthly clinical meeting and luncheon of the Carney Hospital will be held in the auditorium of the Carney Hospital on Monday, November 18, at 11:30 a.m.

PROGRAM

- 1. Business meeting.
- 2. Case reports.
- 3. A New Method of Blood Transfusion: A demonstration.

HARVARD MEDICAL SOCIETY

The next meeting of the Harvard Medical Society will be held in the amphitheater of the Peter Bent Brigham Hospital on Tuesday, November 12, at 8:15 p.m.

PROGRAM

- 1. Presentation of cases.
- 2. The Army in 1941: Contemplated military progress. Lt. Col. W. A. Collier, G.S.C.
- 3. The Practice of Medicine in the Army. Lt. Col. O. H. Stanley, M.C., U. S. A.

BOSTON DOCTORS' SYMPHONY ORCHESTRA

The Boston Doctors' Symphony Orchestra will rehearse under Alexander Thiede, former concertmaster with the Cleveland Symphony Orchestra, every Thursday at 8:30 p.m. Those interested in becoming members should com-

municate with Dr. Julius Loman, Pelham Hall Hotel, Brookline (BEA 2430).

MASSACHUSETTS EYE AND EAR ALUMNI ASSOCIATION

The annual meeting of the Massachusetts Eye and Ear Alumni Association, held in conjunction with the New England Ophthalmological and the New England Otolaryngological societies, will take place on Tuesday and Wednesday, November 12 and 13. The annual meeting and dinner (informal) will be held at the University Club on Wednesday evening, beginning with refreshments and a social gathering at 6:00 p.m.

ESSEX SOUTH DISTRICT MEDICAL SOCIETY

A mental health conference, sponsored by the Essex South District Medical Society and eight other Massachusetts organizations, will be held on Friday, November 15, at the Hotel Hawthorne, Salem, at 9:30 a.m. Luncheon will be served at 1:00 p.m. Dr. Harry C. Solomon will speak on "Diagnosis and Treatment of Mental Disorders."

MASSACHUSETTS TUBERCULOSIS LEAGUE

The midyear meeting of the Massachusetts Tuberculosis League will be held at the University Club, 40 Trinity

Place, Boston, on Thursday, November 14. The theme of the meeting concerns rehabilitation of the tuberculous.

At 10:00 in the morning, Dr. O. S. Pettigill will lead a round-table discussion on rehabilitation cases, and at 11:00 Miss Mabel M. Brown will be chairman of a round-table discussion on employment problems of the tuberculous. Outstanding authorities from the Massachusetts Employment Service, the Division of Vocational Rehabilitation, the Massachusetts National Youth Administration and other agencies will take part in the latter.

At 12:30, luncheon will be served, the charge being \$1.00 per person. The principal speaker will be Miss Jessamine S. Whitney, statistician of the National Tuberculosis Association, who will discuss what is happening to tuberculous patients five years after their discharge from sanatoriums. Since these results include figures from eight Massachusetts sanatoriums and other agencies and organizations, they should be of exceptional value to Massachusetts physicians.

All interested persons are cordially invited to attend the meeting. Reservations can be made by telephoning (HAN 5480) or writing to the office of the Massachusetts Tuberculosis League, 1148 Little Building, Boston.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

The next written examination and review of case histories (Part I) for Group B candidates will be held in the various cities of the United States and Canada on Saturday, January 4, 1941, at 2:00 p.m. Formal notice of the place of examination will be sent to each candidate several weeks in advance of the examination date. No candidate will be admitted to examination whose examination fee has not been paid at the secretary's office. Candidates who successfully complete the Part I examination proceed automatically to the Part II examination to be held in June, 1941.

The general oral and pathological examinations (Part II) for all candidates (Groups A and B) will be conducted by the entire board, meeting at Cleveland, Ohio, from May 28 to June 1, 1941, immediately prior to the opening of the annual meeting of the American Medical Association.

Application for admission to Group A, Part II examinations must be on file in the secretary's office not later than March 15, 1941.

After January 1, 1942, there will be only one classification of candidates, and all will be required to take the Part I and Part II examinations.

The board announces a modification of the case-record ruling (effective January 1, 1942) as it appears in the September, 1940, issue of the booklet issued by the board. This ruling should read: "It is preferable that the number of cases submitted should not be more than half (25) of the total number of fifty (50) cases required."

For further information and application blanks, address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

UNITED STATES CIVIL SERVICE COMMISSION EXAMINATIONS**MEDICAL TECHNICIANS**

Medical technicians experienced in surgical and x-ray work are needed by the War Department. The United States Civil Service Commission has announced an examination to fill these positions in the following grades and optional subjects: senior medical technician (roentgenology), \$2000 a year; medical technician (roentgenology, and surgical), \$1800 a year; assistant medical technician

(roentgenology, and surgical), \$1620 a year. The salaries are subject to a retirement deduction of $3\frac{1}{2}$ per cent.

Applications must be on file with the Commission's Washington office not later than November 28, if received from states east of Colorado and not later than December 1, 1940, if received from Colorado and states westward.

Applicants must have completed a four-year high-school course, unless they pass a written general test, and in addition, they must have had responsible experience in surgical duties in an operating room or clinic, or in x-ray work including x-ray photography and posturing, and in the installation and maintenance of x-ray apparatus. Appropriate college study may be substituted for part of the required experience. With the exception of those who have not completed the high-school course, applicants will not be given a written test. All competitors will be rated on their qualifications as shown in their applications and on corroborative evidence.

Detailed information regarding the examinations and the proper application forms may be obtained from the Secretary of the United States Civil Service Examiners at any first-class or second-class post office or from the United States Civil Service Commission, Washington, D. C.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING SUNDAY, NOVEMBER 10

TUESDAY, NOVEMBER 12

Massachusetts Eye and Ear Alumni Association.

*9-10 a.m. Narcolepsy: A review and presentation of cases. Dr. W. F. Murphy. Joseph H. Pratt Diagnostic Hospital.

12:15-1:15 p.m. Clinicoroentgenological conference. Peter Bent Brigham Hospital amphitheater.

8 p.m. Mechanics of Gas Anesthesia. Dr. Albert Miller. New England Society of Anesthesiology. Boston City Hospital.

8:15 p.m. Harvard Medical Society. Peter Bent Brigham Hospital amphitheater.

8:15 p.m. Recent Advances in the Study of Cancer. Dr. Austin M. Bruce. Greater Boston Medical Society. Beth Israel Hospital auditorium.

WEDNESDAY, NOVEMBER 13

Massachusetts Eye and Ear Alumni Association.

*9-10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*12 m. Clinicopathological conference. Children's Hospital.

12 m. Boston Gastro-Enterological Society. Carney Hospital auditorium.

*2-4 p.m. Diarrhea and Constipation. Drs. E. S. Emery and Robert Zollinger. Peter Bent Brigham Hospital.

THURSDAY, NOVEMBER 14

*8:30 a.m. Combined clinic of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital, at the Peter Bent Brigham Hospital.

*9-10 a.m. Ovulation and the Effects of Pregnant Mares' Serum—Gonadogen (motion picture). Joseph H. Pratt Diagnostic Hospital.

*10 a.m. Massachusetts Tuberculosis League. University Club, 40 Trinity Place, Boston.

FRIDAY, NOVEMBER 15

*9-10 a.m. Ménière's Disease. Dr. Donald Munro. Joseph H. Pratt Diagnostic Hospital.

SATURDAY, NOVEMBER 16

*9-10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*Open to the medical profession.

NOVEMBER 8, 15 and 22—Thomas William Salmon Memorial Lectures. Page 692, issue of October 24.

NOVEMBER 12—New England Society of Anesthesiology. Page 743, issue of October 31.

NOVEMBER 13—Neisserian Medical Society of Massachusetts. Page 743, issue of October 31.

NOVEMBER 13—United States Naval Hospital. Page 743, issue of October 31.

NOVEMBER 13, 14—New England Postgraduate Assembly. Cambridge, Massachusetts.

NOVEMBER 14—Pentucket Association of Physicians. Page 263, issue of August 15.

NOVEMBER 14—American Conference on Industrial Health. Page 42, issue of October 17.

NOVEMBER 15—Massachusetts Society for Mental Hygiene. Page 42, issue of October 17.

NOVEMBER 18—Boston Orthopedic Club. Page 786.

NOVEMBER 18—Monthly clinical meeting and luncheon. Carney Hospital. Page 787.

NOVEMBER 20—Boston Society of Biologists. Page 742, issue of October 31.

DECEMBER 10—New England Society of Anesthesiology. Page 743, issue of October 31.

DECEMBER 27-29—National Convention of the Association of Medical Students, Boston.

JANUARY 4, 1941—American Board of Obstetrics and Gynecology. Page 787.

MARCH 8—American Board of Ophthalmology. Page 201, issue of August 1.

APRIL 21-25—American College of Physicians. Page 1065, issue of June 20.

MAY 21, 22—Massachusetts Medical Society, Boston.

JUNE 2-6—American Medical Association. Cleveland, Ohio.

DISTRICT MEDICAL SOCIETIES

ESSEX SOUTH

NOVEMBER 15—Page 787.

FRANKLIN

NOVEMBER 12.

JANUARY 14.

MARCH 11.

MAY 13.

Meetings will be held at 11 a.m. at the Franklin County Hospital, Greenfield.

SUFFOLK

JANUARY 29—Page 604, issue of October 10.

APRIL 30—Page 604, issue of October 10.

WORCESTER

NOVEMBER 13—Grafton State Hospital, Grafton.

DECEMBER 11—St. Vincent Hospital, Worcester.

JANUARY 8, 1941—Worcester City Hospital, Worcester.

FEBRUARY 12—Worcester State Hospital, Worcester.

MARCH 12—Memorial Hospital, Worcester.

APRIL 9—Hahnemann Hospital, Worcester.

Supper at 6:30 p.m. followed by a business meeting and scientific program.

BOOK REVIEW

The Vasometer System in Anoxia and Asphyxia: A study of the adjustment reactions of the mammalian organism. By Ernst Gellhorn, M.D., Ph.D. and Edward H. Lambert, M.D. 4° paper, 71 pp., with 21 illustrations. Urbana, Illinois: The University of Illinois Press, 1939. \$1.00.

This pamphlet is the result of a long series of experiments by Gellhorn and his associates at the University of Illinois. They have studied the effects on the central nervous system of oxygen-deficient gas mixtures, a condition that they define as "anoxia," and those of the same mixtures when combined with an increased carbon-dioxide tension in the blood, a condition that they define as "asphyxia." There is no clear distinction between anoxia and asphyxia in the medical literature, and the authors have carefully defined their use of these two words. The effects of the mixtures are measured in terms of the blood pressure of anesthetized dogs. They find that the effect of carbon dioxide is increased in anoxia, partly due to the weakening of the carotid-sinus pressor reflexes. Also, it is assumed that the intracellular metabolites formed during short periods of anoxia may interact with the effects of carbon dioxide.

The New England Journal of Medicine

Copyright, 1940, by the Massachusetts Medical Society

VOLUME 223

NOVEMBER 14, 1940

NUMBER 20

SYMPOSIUM ON SUDDEN DEATH

SYPHILITIC AORTITIS AS A CAUSE OF SUDDEN DEATH*

TIMOTHY LEARY, M.D.†

BOSTON

AT NO time in the history of syphilis has so remarkable a change occurred in the character of the disease over a limited period as has been observed in the last few decades. There may be some basis for debate concerning the frequency of incidence of new infections, but there can be no question that the nature of the disease has been greatly modified during this period.

Dramatic types of skin lesions, not unusual a generation ago, have become so uncommon that they are photographed and published as rarities. Most of the extensive skin lesions met with today in syphilitic patients are in the form of dermatitis foliata, due to the treatment, and not to the disease.

Gummatous lesions, common at autopsy in the earlier period, and encountered in surgical specimens, notably those from the testicle, are rare today. The important forms of the disease seen by the pathologist are those which center in the cardiovascular and the central nervous systems. In cardiovascular syphilis, syphilitic aortitis is almost exclusively the lesion found.

Moore,¹ of Baltimore, and those associated with it in the study of the disease in several cities do not believe that modern therapeutic methods are responsible for these changes.

Though the ideal sterilizing agent that Ehrlich hoped to produce has not been found, and though the treponema is not killed so readily as was once believed possible, the uncovering of cases of syphilis by tests of body fluids, and the more general and more intelligent application of treatment, would have been sufficient at least to modify the virulence of the strains of treponemas that trans-

mit the disease, so that less fulminating types of infection should result.

SYPHILITIC AORTITIS

Syphilitic aortitis is a productive vascular disease. Vasa vasorum normally penetrate only to the outer third or at most the outer half of the aortic media. The normal intima is not vascularized, and depends for its nutrition on diffusion through the endothelial layer from the blood flowing through the vessel.

Under the stimulation of the treponema of syphilis the vasa vasorum grow and branch. They extend through the whole of the media and invade the intima. Their growth is associated with a development of fibroblastic tissue. The intima becomes greatly thickened, particularly in the plaques, which are thought to be characteristic of syphilis (Fig. 1). These plaques differ from those of the atherosclerotic type in that in the latter the growth of fibrous tissue is stimulated by the presence of cholesterol, and vascularization is a secondary phenomenon. The lesions tend to encircle the aortic ring, producing the so-called "girdle of Venus" (Fig. 2).

The growth of connective tissue in the region about the aortic ring is important, because the new intimal tissue invades the orifices of the coronary arteries and those portions of the vessel which lie in the aortic wall. The narrowing of one or both orifices and of the lumen within the wall may lead to essential occlusion of this portion of the vessel. In most cases the narrowing of the lumen, though almost complete, is not great enough to prevent microscopic identification of the original lumen (Fig. 3). The occlusion is rarely so complete that it is difficult to distinguish the extremely narrowed normal lumen from the branches of vasa vasorum that are found in the occluding tissue.

*This and the two subsequent papers were presented at a meeting of the Massachusetts Medical Legal Society on February 7, 1940.

†This paper is an abstract from the Friedlander Lecture, delivered before the Greater Cincinnati Heart Council, November 14, 1939.

1Medical examiner, Suffolk County, lecturer in legal medicine, Harvard Medical School, professor of pathology (emeritus), Tufts College Medical School.

In some cases, as Moritz² has shown, the lesions may extend for short distances beyond the portions of the coronary arteries within the aortic wall.

The invasion of the coronary ostia is slow, and a collateral circulation to the heart, by anastomoses with pericardial vessels, bronchial arteries and the

occurs before extension over considerable regions of the aorta has come about.

When the coronary orifices are not particularly narrowed, early sudden death does not occur. Under these conditions the lesions usually extend progressively up the aorta over the arch and down the thoracic aorta. In most cases they terminate

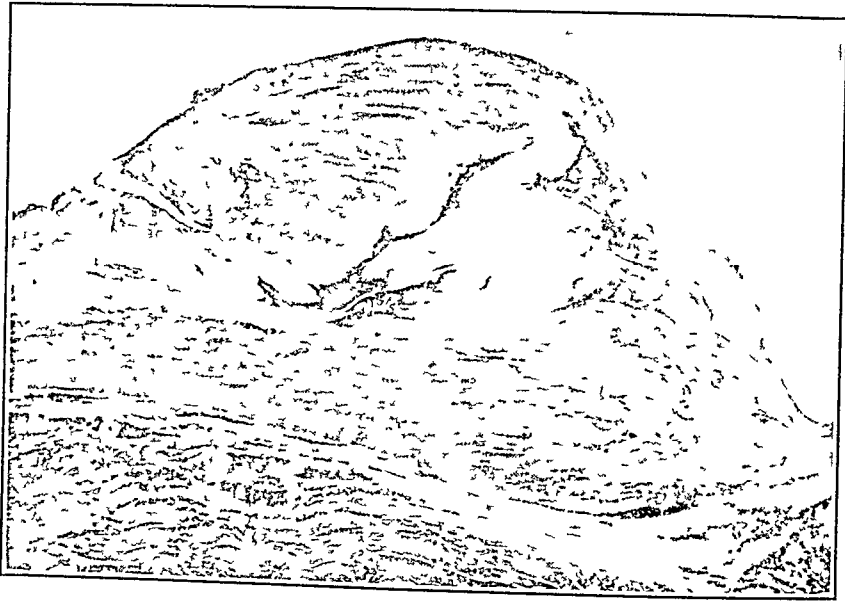


FIGURE 1. Frozen Section through an Early Syphilitic Plaque at the Aortic Ring.

Vessels originating in the vasa vasorum have burgeoned up through the media and, with secondary growth of fibroblastic tissue, make up the intimal plaque. The vessels are surrounded by a veil of lymphoid cells. Productive endarteritis has occluded some of the branches, and regions of necrosis (dark) have been produced. Note the thick-walled vasa vasorum below.

aortic vasa vasorum, carries on the coronary blood supply, as Wearn³ and others have shown. This is well illustrated in cases in which the coronary lumen is essentially obliterated as it passes through the aortic wall, but on its emergence from the wall is found to be of normal caliber. The abrupt change from an essentially obliterated lumen to a vessel of normal caliber and normal wall implies that a circulation quantitatively approaching the normal has been continued. However, it is a substitute circulation, and therefore subject to emergency hazards.

Perhaps because of the cutting down of coronary pressure by the narrowing or occlusion of the coronary ostia, the coronary arteries in syphilitic aortitis show less atherosclerosis than is usual at given ages. Syphilitic lesions of the coronary vessels, apart from the region about the ostia, are unusual.

Serious narrowing of the coronary orifices is associated with the early stages of syphilitic aortitis. Because of the interference with the coronary circulation, sudden death, of coronary type, usually

with striking abruptness at the level of the diaphragm. A normal-appearing aorta connects directly along a more or less transverse line with the active syphilitic lesion.

Rupture through the redundant and necrotic intimal tissue in the ascending aorta above the ring may give rise to focal dissecting aneurysms, which usually rupture into the pericardium and thus produce sudden death. The scarred media of syphilis does not lend itself to the separation of its layers by blood which has torn its way through the intima, so that typical, long, dissecting aneurysms are not produced.

In the later stages, usually many years after the primary infection, the syphilitic process tends to lead to aortic insufficiency. This may be produced by widening of the commissures where the valve cusps meet. Or it may be due to involvement and narrowing of the cusps by the thickening and rolling in of their edges. In general, however, these factors are much less important than the relaxation of the aortic ring as a whole.

Marked relaxation of the ring is rarely due to syphilis alone. Damage to the aortic media as the result of syphilis is usually focal, and may produce essential destruction of the media in these regions, including both muscle and elastic layers. This is accompanied by fibrosis, but the fibrous tissue tends to be less stable than the normal media,

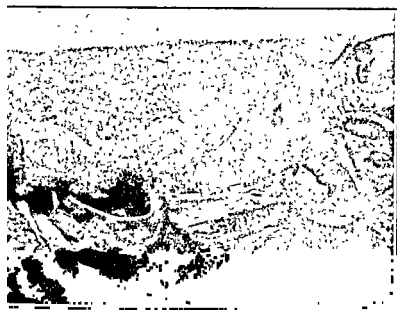


FIGURE 2. "Girdle of Venus" about the Aortic Ring in a Woman of Thirty-three Years, Found Dead.

The right coronary orifice is occluded. The left coronary orifice is marked by a dimple. The left coronary artery beyond the occlusion in the aortic wall, as seen at the right of the photograph, is normal.

The aorta undergoes dilatation through the wear and tear of use. As a result of focal damage to the media, aneurysms may be formed, saccular if the effective damage to the media is sharply focal, fusiform if it is more extensive. The rupture of an aneurysm may of course be the cause of sudden death, though, according to Weiss,⁴ aneurysms of syphilitic origin are becoming less frequent.

Diffuse dilatation of the aorta, including the ring, is usually due to a combination of syphilitic aortitis and atherosclerosis. The normal-ascending aorta is resistant to the production of advanced atherosclerotic lesions. On the other hand, it is frequently the site of multiple small atheromatous nodules. These lesions may spread locally from the initial pinhead deposits of lipid cells to fan-like extensions which cover large portions of the ascending aorta. The lipid cells are limited to the intima. The lesions remain superficial because

the removal of the lipid from the surface lesions by fibroblastic cells, as I have demonstrated.⁵ The early orange-colored lesions become pale yellow, then gray, and finally flatten out and disappear. Though fibroblastic tissue is formed in these lesions, it produces little or no collagen and therefore causes no scarring.

In the syphilitic aorta this defense of the ascend-

ing aorta against atherosclerosis is no longer active. In fact, syphilitic aortitis favors the invasion of lipid cells, which are not limited to the internal layer of the intima but enter the deeper layers of the thickened intima and the media. Examination of frozen sections discloses that lipid cells not only invade the aorta through the surface endothelium, as is true in atherosclerotic processes in general, but also directly invade the deep layers through the vasa vasorum. The result of the ready access of lipid cells in the syphilitic aorta is the production of more continuous atherosclerotic lesions in the upper aorta than are met with under other conditions. Syphilitic lesions alone are not particularly prone to give rise to calcification, although small calcified foci may arise. Atherosclerotic lesions commonly undergo calcification. As a result of the combined syphilitic and atherosclerotic processes, calcification, particularly of the

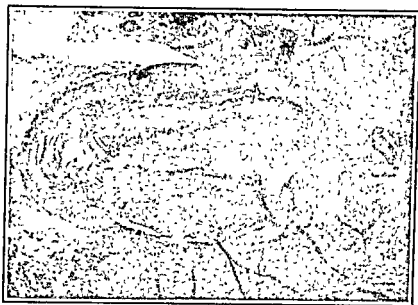


FIGURE 3. Tangential Section through the Aortic Wall across an Essentially Occluded Coronary Artery.

The oval contour of the vessel is indicated in part by the coronary media. Connective tissue from the aortic intima is occluding the lumen, except for a small slit along the medial junction below.

ascending aorta and arch, may be practically continuous. The atherosclerotic process comes to dominate the picture in late lesions. As the effects of syphilis wane with age, the atherosclerosis waxes.

More important than calcification is the diffuse dilatation, which is almost constant in an aorta that is the seat of the combined processes. As indicated, it usually includes the ring, and is responsible for most of the aortic insufficiency met with in late syphilitic aortitis (Fig. 4). So-called "senile atherosclerosis" with continuous dilatation and calcification of the upper aorta is almost constantly engrafted upon syphilitic aortitis.

Aortic insufficiency may be responsible for sudden death because of its effect on the cardiac

blood supply. The main coronary circulation occurs during diastole. During systole the contracting ventricular muscle compresses the muscular branches of the vessels. In most animals a recognizable pallor of the ventricular muscle is produced in systole. With the closure of the aortic cusps and the relaxation of the ventricular muscle, circulation is favored. When the closure is

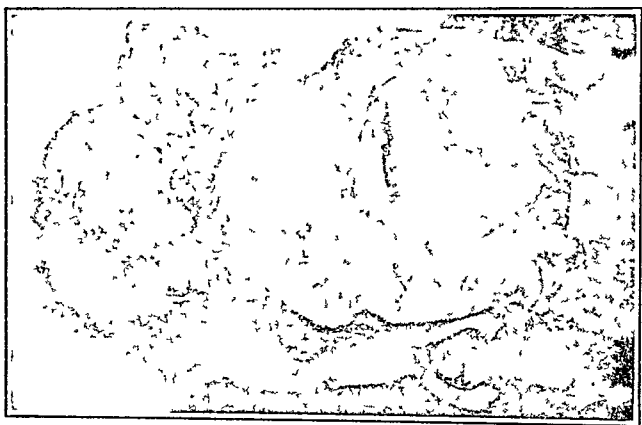


FIGURE 4. *Aortic Ring, Ascending Aorta, Aortic Arch and Portion of the Thoracic Aorta.*

Universal atherosclerosis, grafted on a syphilitic base, has resulted in generalized dilatation and redundancy of the aortic ring and wall. Death occurred from aortic insufficiency.

inadequate there is leakage back into the left ventricle and, what appears to be more significant, a loss of tonus in the circulatory system in advance of the lesion. As a result, coronary circulation is inadequate, and decompensation or sudden death may be the outcome. Most commonly, however, the victims of this condition are hospitalized and die from progressive decompensation.

In addition to stimulation of vessel growth a characteristic endarteritis of the vasa vasorum is produced, which gradually cuts down the blood supply to the new intimal vessels and results in necrosis and scarring of the redundant intimal tissue. The signs of syphilitic aortitis persist for years in the form of productive endarteritis of the vasa vasorum, lymphoid-cell infiltration and scarring of the adventitia, together with medial scarring. Because of these lesions, the disease can be identified even in patients of advanced age. The characteristic intimal wrinkling also persists for years, but may ultimately smooth out in large part.

In this connection it is interesting to record some results of late experimental atherosclerosis in the rabbit that reproduce the picture of diffuse dilatation of the aorta seen in combined syphilitic and atherosclerotic processes, and support the evidence that such dilatation is the result of the associated atherosclerosis in this combination (Fig. 5).

If rabbits are fed cholesterol to the point of producing high-grade aortic atherosclerosis, and are then allowed to live for several years, the aorta exhibits diffuse dilatation starting around the ring and including, in most cases, the arch and the thoracic vessel. This dilatation is usually associated with calcification, which is frequently continuous.

The ascending aorta in the rabbit does not possess the resistance to atherosclerosis shown in man, or else the continued heavy dosage of cholesterol overcomes any resistance that may have existed. The lesions therefore extend continuously from the ring along the aorta, as in human atherosclerotic lesions secondary to syphilitic aortitis, and undergo dilatation and calcification, as do the combined human lesions.

That syphilitic aortitis is a serious disease even when it gives rise to aneurysm, or affects the cor-

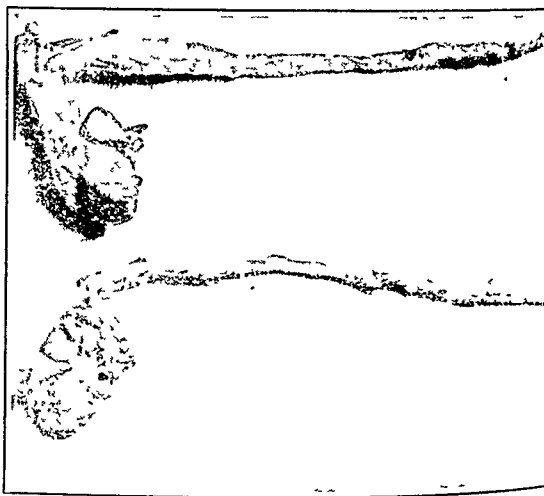


FIGURE 5.

The upper heart and aorta are from an atherosclerotic rabbit that was first fed cholesterol in 1934 and died in 1939; the lower heart and aorta are from a normal rabbit.

nary blood supply through the lesions about the ring, is illustrated by a recent autopsy on my service. A woman sixty-nine years of age was killed by an automobile. Death was due to a fractured skull and chest injuries. A casual finding at autopsy was a syphilitic aortitis combined with arteriosclerosis. The lesions were unusual in that they arose well above the aortic ring. Although the aorta showed the typical diffuse dilatation along the site of the lesions, there was no dilatation of the ring. The other organs showed no evidence of syphilis and were well preserved, considering the patient's age. In other words, there was nothing to indicate that the syphilitic aortitis had had any measurably harmful effect on her physical condition.

The limitation of the process above the aortic ring is responsible for its relative innocuousness.

SUMMARY

Syphilitic aortitis is associated with overstimulation of the essential aortic blood vascular system, the vasa vasorum. With the excessive growth of blood vessels, which penetrate through the media into the intima, there is an excessive growth of fibroblastic tissue, which thickens the intima and tends to narrow and occlude the portions of the coronary arteries lying within the aortic wall. Marked narrowing or occlusion of the ostia may result in sudden death, of coronary type, in the early stages of the disease.

In addition to widening of the commissures and rolling of the cusps, the association of atherosclerosis with late syphilitic aortitis tends to be followed by calcification and diffuse dilatation of the aorta, including the ring. Dilatation of the ring produces aortic insufficiency, which may be followed by sudden death, of coronary type, but usually leads to late progressive cardiac decompensation. Rupture of aneurysms is also a cause of sud-

den death, as is the production of local dissecting aneurysms in the lower ascending aorta, with rupture into the pericardium.

Experimental atherosclerosis in the rabbit following the feeding of cholesterol results in late diffuse dilatation of the aorta resembling that found in combined syphilitic aortitis and atherosclerosis in man.

I am indebted to Dr. Frederic Parker, Jr., for access to syphilitic material from the Boston City Hospital collection, and to Dr. Tracy B. Mallory for microscopic preparations from the Massachusetts General Hospital collection. My own service has been rich in early lesions, with sudden death due to occlusion of coronary ostia, and in late combined atherosclerotic and syphilitic lesions, with dilatation of the ring producing sudden death from aortic insufficiency.

784 Massachusetts Avenue

REFERENCES

1. Moore, J. E. personal communication.
2. Moritz, A. R.: Syphilitic coronary arteritis. *Am. J. Path.* 11:44-59, 1931.
3. Weirn, J. T.: The extent of the capillary bed of the heart. *J. Exper. Med.* 47:273-291, 1925.
4. Hudson, C. L., Moritz, A. R., and Weirn, J. T.: The extracardiac anastomoses of the coronary arteries. *Ibid.* 56:919-925, 1932.
5. Weiss, S.: Dissecting aneurysm of the aorta. *New Eng. J. Med.* 218:512-517, 1938.
6. Leary, T.: Atherosclerosis. *Am. J. Path.* 21:419-462, 1936.

INSTANTANEOUS "PHYSIOLOGIC" DEATH*

SOMA WEISS, M.D.†

BOSTON

POST-MORTEM examination of the body, the time-honored method for seeking the cause of death, continues to be the most valuable means of approaching this question. The use of physical and chemical methods in post-mortem investigation often reveals additional essential information that cannot be obtained simply from morphological analysis. It should be emphasized, however, that post-mortem study alone does not always give a precise explanation of the exact mechanism of death. The structural changes found at necropsy usually disclose only an underlying disturbance or damage which makes the cause of a certain type of death plausible. There are cases in which observations made during life by clinical, physiological and chemical methods are of more value than is post-mortem examination in establishing the specific mechanism of death. In clinicopathological correlations, the data obtained with the aid of physi-

ological and chemical methods are becoming more and more important.

One of the most perplexing problems facing both physicians and pathologists is the explanation of instantaneous death. The term "sudden death" is frequently used to describe the unexpected occurrence of death within a space of several minutes or even hours after the onset of alarming symptoms. Often death is called sudden if a person is found unexpectedly dead as the result of natural causes, but with the mode of death and duration of symptoms unknown. Under such circumstances the symptoms could have been present for hours or possibly longer. It is of interest that Martland¹ found that in 2000 necropsies on cases of sudden death 84 per cent of the dead persons were males and that the most frequent structural lesion found was coronary disease. This is particularly significant because the incidence of hypertension, often assumed to be one of the main causes of coronary disease, is higher in women than in men. The underlying diseases and mechanisms of sudden death are multiple; coronary dis-

*Presented at a meeting of the Massachusetts Medico-Legal Society, Boston, February 7, 1940.

†From the Medical Clinic, Peter Bent Brigham Hospital, and the Department of Medicine, Harvard Medical School.

†Hester, Professor of the Theory and Practice of Physic, Harvard University, physician in chief, Peter Bent Brigham Hospital.

case in particular and other types of heart disease, cerebrovascular accidents, pulmonary embolism, dissecting aneurysm of the aorta, internal hemorrhage, obstruction of the trachea and various types of poisoning are mainly responsible. Although in the large group of cases with sudden death an underlying organic disease of the vital organs is found post mortem, it should be remembered that in other persons structural damage of equal or greater severity may be compatible with good functional capacity. Hence the precise cause of death often remains unexplained by the pathologist. Under such circumstances his finding of "sudden death from natural causes" is based on a clinicopathological correlation which has taught us that in the presence of certain types of organic heart disease sudden death may occur. Why, with the same degree of structural damage present, sudden death occurs in one person and not in another, *remains unanswered.*

If from the entire group of cases with sudden death one selects a subgroup in which death occurred without warning symptoms and practically instantaneously, usually in a matter of seconds rather than minutes or hours, one finds, at least in my experience, that in the majority of cases acute structural lesions in vital organs are often meager or absent. The lesions offered as an explanation of death are usually chronic. Post-mortem examination, as a rule, fails to reveal proof of or even evidence for the cause of death. Although physicians and students usually suspect cerebral hemorrhage, pulmonary embolism or fresh coronary thrombosis, generally such findings are not corroborated by the pathologist.

The mechanism of instantaneous death has been little studied. It is remarkable how seldom the physician or nurse observes its occurrence, or that of brief, transient, alarming seizures, including syncope. Thus, I examined the hospital records of 230 patients suffering from attacks of various types of syncope, and found that in no case were the episodes observed by physicians or nurses.

We have been interested in the mechanism of instantaneous death for the last seven years in connection with studies on syncope, collapse and shock.²⁻¹⁴ Our observations indicate that instantaneous death is usually cardiac in origin, and that its occurrence depends on an underlying physiologic mechanism. There is a close similarity and interrelation between the mechanism of instantaneous death and that of syncope; frequently, indeed, instantaneous death is merely fatal syncope. Thus it is interesting that in a study of fifty cases of aortic stenosis most of the patients who suffered from attacks of syncope died

instantaneously. It is known, too, that patients suffering from the Adams-Stokes type of syncope may die instantaneously during one of their usual attacks. The mechanisms of transient and fatal syncope are presumably similar or identical in these cases.

A systematic study of syncope has revealed that the physiologic mechanisms responsible for these transient attacks of unconsciousness vary. I have differentiated twelve types of syncope. In determining the general tendency to syncope, changes in reflexes and in the myocardium play a fundamental role. Increased irritability of the afferent or efferent nerve endings or the central synapses produces hyperactivity of these reflexes. The sensitizing factors may be merely transient, such as emotional or chemical (including nutritional) agents, or persistent, usually due to structural changes. In cardiac syncope increased sensitivity of the myocardium and nerve structures within, caused by ischemia and infections, plays an important part. Conditions like coronary sclerosis, the myocardial hypertrophy of arterial hypertension, aortic stenosis and various types of infectious myocarditis or nutritional deficiencies are factors that predispose both to syncope and to instantaneous death, for in these states the heart has a general tendency to asystole or to cardiac arrhythmias. Such cardiac dysfunction can be induced by the stimulation of various reflexes. Thus, we have observed and been able to induce reflex reactions of asystole, auricular fibrillation, bundle-branch block and complete auriculoventricular dissociation. At no time did we observe the occurrence of ventricular fibrillation of reflex origin. In the presence of coronary sclerosis there is a tendency to hypersensitivity of the vagal type of carotid-sinus reflex as well as of other vagal reflexes. We observed a patient, for example, who developed such high sensitivity of the carotid-sinus reflex following coronary thrombosis that turning the head or gentle manipulation of the skin of the neck close to the carotid sinus induced alarming transient asystole. Irritation of nervous structures in the orbit, tonsils, neck, mediastinum, esophagus, trachea, bronchi, pleura, peritoneum, stomach, gall bladder and other organs due to inflammation, tumor or other changes can induce alarming syncopes and, rarely, instantaneous death. We^{3, 15} have pointed out elsewhere that in normal persons the tonus and activity of the reflexes of the autonomic nervous system vary considerably. Under the influence of stress and strain or of disease, a remarkable degree of hyperactivity of selected reflexes can develop. This explains the otherwise puzzling fact that although in many persons

the effect of emotion or chemical stimuli on the heart and vessels is slight, and surgical manipulation of certain nerve structures can be one with safety, in a few cases such stimulation precipitates an alarming seizure or death.

The essential difference between syncope in health and in certain diseased states lies in the ability of the patient to re-establish normal equilibrium. Whereas in normal subjects, owing to the action of numerous emergency functions and to the reserve capacity of the organs involved, a return to the normal cardiovascular equilibrium is accomplished with relative ease and promptness, in diseased persons, because of damaged systems of organs, a return to the normal level is more difficult, usually slower and may not even occur.

The circulation in syncope is influenced markedly by gravity. Hence the circulatory disturbance is particularly severe in the orthostatic position, and the maintenance of this position during syncope or collapse in the presence of a hyperirritable myocardium becomes a serious threat to the patient's life. Thus pleural, pericardial or abdominal tap in patients with myocardial disease is more apt to lead to instantaneous death in a sitting position than in a recumbent one. Patients with an ischemic myocardium or with hyperactive vagal reflexes are apt to die instantaneously during the strain of defecation.

We have pointed out that it is more than a coincidence that cerebral ischemia is one of the stimuli effective in bringing on unconsciousness, abolishing voluntary muscular activity, and causing convulsive movements. The combined effect of these changes is an improved return of blood to the heart and to the brain. Our studies indicate that such stimulation or inhibition of the central regulation of consciousness and the convulsive centers usually develops long before there is any damaging effect from cerebral anoxia. Thus in discussing the role of the carotid-sinus reflexes in health and in disease we³ have stated:

The teleological explanation offered for the location of the carotid-sinus reflex is that it is placed at the point of entrance of the arterial blood column into the brain, a vital organ most sensitive to fluctuations in the circulation, in order to maintain a constant blood supply at an optimal pressure. It is perhaps more than a coincidence that the same mechanism was also found to be closely related to the central regulation of unconsciousness and convulsions. These two functions may also be looked upon as emergency measures for the maintenance of an adequate blood supply to the brain. The occurrence of unconsciousness inhibits many activities leading to fluctuation of the cerebral blood flow, and in addition the change in position of the brain and body from the upright to the horizontal adds a further factor of safety to the cerebral blood supply. Convulsions, on the other hand, are an effective mechanism

for improving the blood flow to the brain in the presence of vasomotor failure and may be looked upon as an accessory emergency mechanism in the presence of unconsciousness. Thus the data here presented expand the protective regulatory influence of the carotid-sinus mechanism on cerebral functions, although the exact nature of the change in the cerebral centers is not clear. That this protective cerebral function is submerged in health and can become purposeless or even harmful in certain abnormal states of the carotid-sinus mechanism is in complete harmony with the behavior of numerous other regulatory mechanisms in human beings.

Instantaneous death is prone to develop in either young or elderly patients after exertion if the vital reflexes and the myocardium are irritable. During the administration of a volatile anesthetic instantaneous death may be caused by hyperactivity of the cardiac reflexes induced by a certain stage of the anesthesia. Instantaneous death may occur, too, during angina pectoris, but if it occurs without warning, formation of fresh thrombosis attributable to such death is usually not found post mortem. Following coronary thrombosis, however, instantaneous death may occur at any time, and again, fresh structural changes referable to instantaneous death are not found. Although rarely rupture of the heart following thrombosis may lead to instantaneous death, usually, as in other types of cardiac tamponade, this does not occur. In the presence of ischemic myocardium and hyperactive reflexes, fright or other emotional stress may induce cardiac arrhythmia, syncope and death.

It is often stated that ventricular fibrillation is the underlying physiologic state in the causation of instantaneous death. The evidence for such a claim, however, is lacking. Although ventricular fibrillation may occur unexpectedly and usually causes syncope,¹⁶ in our experience this arrhythmia plays but a minor role in the causation of unexpected states of unconsciousness. It is of interest that asystole occurs more frequently than ventricular fibrillation in the usual types of death due to infectious or degenerative diseases.^{17, 18}

The following cases are presented briefly as examples of instantaneous death.

CASE 1. J. J. M., a 63-year-old man, was admitted to the Peter Bent Brigham Hospital on December 2, 1939. There was a history of rheumatic fever years previously. No history of angina or physical incapacity could be elicited. The patient worked daily until the day of admission. Shortly before noon of that day he noticed a dull, aching pain in and about the left shoulder. He continued to work in the afternoon, when some distress was experienced in the left arm, radiating down to the left elbow. On his way home in the evening he felt uncomfortable and oppressed by the heat in the crowded streetcar. After walking several hundred feet he lost consciousness and fell. A friend, observing frothing at the mouth,

thought that the attack was an epileptic fit, and brought him to the hospital.

On examination the heart was fibrillating. A soft, mid-diastolic apical rumble was heard. The rest of the examination was essentially negative. The white-cell count was 12,500. The urine contained a heavy trace of sugar. The electrocardiogram revealed paroxysmal auricular fibrillation, but otherwise was normal. The patient was quite comfortable after admission. The leukocyte count fell to 9000 the next day, but rose again to 16,000. Four hours after admission the heart action became regular, and the rate was 60 per minute. The following day the electrocardiogram and the blood pressure were both normal. The patient felt so well that he wished to leave the hospital. Fifty-four hours after the onset of symptoms, while two nurses were taking the heart rate routinely, one listening to the heart and the other taking the pulse rate, the patient, though previously cheerful and comfortable, suddenly died with no moan, cry or convulsion. His eyes simply became glassy. The occurrence of death was described as follows by a nurse:

When we entered the room to take the 4 o'clock apex rate, the patient talked to us and seemed to be in good condition. I was taking the apex rate when I noted a sudden change in sound and rhythm. For the first 45 seconds of the minute I heard a regular, moderate beat, but suddenly, almost with a bang, it became very loud and somewhat irregular. We continued counting for the full minute, but because of the strange rhythm and loudness I continued to listen for a couple of seconds. The patient was staring ahead with glassy eyes. I spoke to him, but he did not respond. Dr. R. was called and arrived right away. By that time the patient was quite cyanotic. Adrenalin was administered, but there was no response.

The necropsy examination revealed that the pericardial sac contained 650 cc. of blood. On the lateral wall of the left ventricle, extending up 6 cm. from the apex, there was a fresh infarction containing a slit-like perforation 2 to 3 mm. long. There was also an old healed mitral stenosis. The coronary arteries were sclerosed, with almost complete occlusion of the descending branch of the left circumflex artery.

Comment. This case is of special interest because rupture of the heart occurred within as short a time as 54 hours after the onset of symptoms of coronary thrombosis, and it was possible to observe the action of the heart during its rupture. Death was instantaneous and was preceded only by the development of cardiac arrhythmia of 15 to 20 seconds' duration. Usually death in cardiac tamponade is not instantaneous.

CASE 2. J. F., a 60-year-old man, was admitted to the Peter Bent Brigham Hospital on November 3, 1939. He had contracted syphilis, with a penile chancre, 28 years previously. Twelve years previously he had experienced three spells of unconsciousness. For 15 years on and off he had experienced slight dyspnea on exertion, but no other evidence of heart disease could be elicited. Symptoms of classic tabes had been present for 10 years, with boring pains along the extremities, failing vision, abnormal gait and incontinence of urine and feces particularly prominent.

Examination revealed Argyll-Robertson pupils. The speech was slurred. The heart was normal. The blood pressure was 180/75. Bone conduction of the vibration sense was absent. The pain, touch and temperature sensations were slightly diminished. The Romberg test was positive. The blood Wassermann and Kahn tests were posi-

tive. There was a moderate degree of secondary anemia. The other tests were noncontributory. Following malaria therapy the blood pressure fell to about 115/65. The patient was allowed to get up and his condition was considered satisfactory, but while resting in bed comfortably he died instantaneously. The death was described by the house physician as follows:

The patient was sitting upright in bed talking to his wife when he suddenly began to breathe slowly, noisily and deeply. I saw him within a matter of seconds after his wife called for aid. The head was turned to the left, the eyes were closed, and the respirations very deep and jerky, 3 or 4 per minute. The face was flushed, and the extremities warm; the pulse was imperceptible, the heart sounds inaudible. After about a minute the deep respirations ceased, only to be replaced by an occasional short gasp accompanied by gurgling in the back of the throat. He was placed in the supine position, and oxygen therapy, artificial respiration, and the intramuscular administration of epinephrine and coramine were instituted. Within 2 or 3 minutes the patient was cyanotic, then ashen, and the extremities became cold. At no time were heart sounds heard.

Post-mortem examination revealed a moderate degree of syphilitic aortitis, sclerosis of the coronary arteries and chronic myocardial fibrosis.

Comment. This case is typical of instantaneous death. A patient with symptomless coronary sclerosis and some myocardial degeneration, but with good functional capacity of the heart, died instantaneously while resting in bed. The degree of structural changes found post mortem were of the type often described in other cases as non-contributory findings.

CASE 3. H. B., a 5½-year-old girl, was admitted to the Children's Hospital on December 1, 1939. She was seen while under the care of Dr. Bronson Crothers, with whose permission the case is reported. On the previous October 26, while ether anesthesia for tonsillectomy was being induced, the patient suddenly stopped breathing and respiration was re-established with some difficulty after artificial stimulation. When the ether anesthesia was resumed the respiration again ceased, and coramine and other stimulants were needed to re-establish it. No further attempt was made to perform the operation. No mention was made on the record of the heart action during these attacks. The patient was readmitted because of retarded development, difficulty in balance during locomotion and two additional convulsive seizures since October 1.

On examination the heart was slightly enlarged. There was a fairly pronounced systolic murmur over the apex and base. The first sound was occasionally accentuated, and an extra sound was heard over the base at irregular intervals. On admission the heart rate was 88, but subsequently it was found to be 44. The electrocardiogram revealed heart block with complete auriculoventricular dissociation. X-ray examination revealed a slightly enlarged heart. Blood serological tests were negative.

It was evident that the patient was suffering from heart block, but its cause was not clear. Some of the physicians who saw her suggested congenital cardiac defects, but to me an obscure myocardial infection seemed plausible. Ephedrin therapy was instituted.

While in the hospital the patient suffered from numerous Adams-Stokes attacks. At times the heart rate dropped to 34 or lower. These attacks came without warning, at times while the patient was playing or running. With a short cry she would collapse, become unconscious and

develop apnea with convulsions. In these attacks heart sounds were absent, or heard only at long intervals. The duration of the attacks varied from several seconds to a few minutes.

On December 23 the patient suffered a severe attack lasting 7 minutes. For several minutes the heart beat was not heard nor the pulse felt. She became intensely cyanotic. Artificial respiration had to be instituted for 15 minutes and coramine was administered. After this attack there were numerous shorter ones. Between attacks the patient felt well and cheerful. On January 8 she became unconscious, developed convulsions and died despite all efforts at resuscitation.

Necropsy failed to explain either the heart block or the cause of death. The heart weighed 150 gm. The chambers were somewhat dilated. Congenital lesions were not present. There was some edema and slight degeneration of the myocardium.

Comment. This patient developed Adams-Stokes attacks, presumably after some infection, and died during one of the attacks. Even after detailed histological study of the heart, including the conductive system, post-mortem examination failed to reveal a specific underlying morphologic lesion. It has been emphasized elsewhere¹⁹ that in influenza and other types of respiratory infection may at times be followed by severe transient or even permanent damage to the myocardium.¹⁰ This type of myocardial disease may be associated with disturbances of the intracardiac conduction and changes in the heart rate and rhythm. It is probable that one can place in this category instantaneous deaths occurring after exertion in robust persons, where post-mortem examination fails to reveal any recognized cause of death. It is of interest that in a recent report on anatomical findings after sudden death, Lisa and Hart²⁰ point out the frequency of respiratory infections associated with myocarditis. Sudden death in childhood is often explained on the basis of status lymphaticus. If this condition exists at all it explains but a few cases of instantaneous death in children.

Of the 3 cases here reported, Case 1 represents instantaneous death, the underlying cause of which was adequately explained by post-mortem study. In Case 2, the post-mortem examination did not explain the cause of death, but the finding of coronary sclerosis indicated myocardial ischemia and hyperirritability as the probable cause. In Case 3 only a slight degree of structural damage was found, but the clinical and electrocardiographic observations offer adequate explanation for the underlying physiologic mechanisms of death.

SUMMARY AND CONCLUSIONS

In cases of sudden death, post-mortem examination frequently fails to explain the mechanism of death. In the majority of cases the underlying structural lesions are chronic, and lesions of the

same type may be found in cases in which they do not contribute to the cause of death. In cases of instantaneous death fresh lesions responsible for death are often absent. In the causation of instantaneous death a hyperirritable myocardium of anoxic or infectious origin and hyperactive reflexes singly or in combination play the most important roles. The functional capacity of the heart before death in these cases may be adequate or good. The determining factor in instantaneous death is often physiologic.

The general nature of syncope is discussed. Evidence favors the concept that instantaneous death is often a fatal syncope. Asystole of various types and ventricular fibrillation are the usual causes.

REFERENCES

- 1 Martland H S unpublished data.
- 2 Weiss S and Baker J P. The carotid sinus reflex in health and disease: its role in the causation of fainting and convulsions. *Medicine* 12:297-354 1933.
- 3 Ferris E B, Jr, Capps R B and Weiss S. Carotid sinus syncope and its bearing on the mechanism of the unconscious state and convulsions. *Medicine* 14:377-456 1935.
- 4 Weiss S, Capps R B, Ferris E B, Jr and Munro D. Syncope and convulsions due to a hyperactive carotid sinus reflex: diagnosis and treatment. *Arch Int Med* 58:407-417 1936.
- 5 Ferris E B, Jr, Capps R B and Weiss S. Relation of the carotid sinus to the autonomic nervous system and the neurones. *Arch Neurol & Psychiat* 37:365-384 1937.
- 6 Weiss S, Ferris E B, Jr and Capps R B. The influence of reflexes in the induction of intracardiac disturbances. *Tr Am Physicians* 49:177-186 1934.
- 7 Weiss S. Syncope and related syndromes. *Christian's Oxford Medicine* Vol 2. New York: Oxford University Press 1935. Pp 250 (9 66).
- 8 Weiss S and Wilkins R W. Syncope collapse and shock: their medical significance and their treatment. *M Clin North America* 21:481-510 1937.
- 9 Weiss S, Wilkins R W and Haynes F W. The nature of circulatory collapse induced by sodium nitrite. *J Clin Investigation* 16:381-1937.
- 10 Wilkins R W, Haynes F W and Weiss S. The role of the venous system in circulatory collapse induced by sodium nitrite. *J Clin Investigation* 16:85-91 1937.
- 11 Wilkins R W, Weiss S and Haynes F W. The effect of epinephrine in circulatory collapse induced by sodium nitrite. *J Clin Investigation* 17:41-51 1938.
- 12 Stead E A, Jr, Kunkel P and Weiss S. Effect of pitressin in circulatory collapse induced by sodium nitrite. *J Clin Investigation* 18:673-678 1939.
- 13 Kunkel P, Stead E A, Jr, and Weiss S. Effect of pargolol (a N dimethyl p hydroxyphenethylamine) on sodium nitrite collapse and on clinical shock. *J Clin Investigation* 18:679-685 1939.
- 14 Weiss S. The regulation and disturbance of the cerebral circulation through extracerebral mechanisms. *A Research Nerv & Ment Dis* Proc 18:571-604 1938.
- 15 Weiss S and Sprague H B. Vagal reflex irritability and the treatment of paroxysmal auricular tachycardia with ipocane. *Am J M Sc* 194:54-63 1937.
- 16 Schwartz S P and Jexer A. Transient ventricular fibrillation: clinical and electrocardiographic manifestations of syncope in patient with auriculoventricular dissociation. *Arch Int Med* 50:450-460 1932.
- 17 Hanson J F, Purks W A and Anderson R G. Electrocardiographic studies of the dying human heart with observations on intracardiac injection of epinephrine: report of twenty five cases. *Arch Int Med* 51:965-977, 1933.
- 18 Sgler L H, Stein I, and Nash P I. Electrocardiographic changes occurring at death. *Am J M Sc* 194:356-369 1937.
- 19 Weiss S. Diseases of the heart and aorta which are not well recognized. *M Clin North America* 23:1313-1344 1939.
- 20 Lisa J R and Hart J F. Anatomical observations on seventy hospital patients after sudden death. *Arch Int Med* 64:43-48 1933.

SUDDEN DEATH*

ALAN R. MORITZ, M.D.†

BOSTON

ABOUT half the cases of death referred to the medical examiner come to him because the cause of death is unknown, rather than because there is positive evidence of violence or foul play. They include not only deaths in which the fatal seizure is sudden and unexpected, but also those in which the cause of death is obscure because no physician was in attendance during the terminal illness.

The primary function of the medical examiner is to investigate deaths in order that murder shall not pass unrecognized. One of the most difficult problems confronting the medical examiner is to decide which cases of sudden or obscure death shall be investigated, and to what extent, in order that deaths from unnatural causes shall not be overlooked.

Contributing to the difficulty of the problem is the fact that mechanical violence may and frequently does cause death without leaving any external evidence of trauma. The patient may die hours or even days after the injury has been sustained. During the interval between injury and death there may be a symptom-free period so that neither the victim nor his friends realize that anything is wrong. If no one knows or tells of such an injury, death is likely to be regarded as having resulted from natural causes. Victims of such internal injuries may be found dead at the scene of the accident or assault, or may collapse some time later while at work or at home.

Fatal injuries of the head, particularly if the scalp is protected by heavy hair or a head covering, are frequently sustained with no external evidence of trauma. Moreover, fatal head injury is often incurred without skull fracture. Death may take place days or months later and the victim may not even have lost consciousness at the time of the injury. Fatal non-penetrating injuries of the chest or abdomen are often sustained without any superficial evidence of their occurrence. Laceration of the liver or spleen or rupture of a hollow viscus is likely to result in fatal hemorrhage or infection hours or days after the trauma. A blow over the heart, the solar plexus or the upper pole of a kidney may be instantly fatal without bruising the skin or fracturing a

rib. Fatal penetrating wounds produced by slender instruments—an icepick or hatpin—are easily overlooked on external examination, and death may not occur for a considerable time after the assault.

The medical examiner must judge each case on the evidence presented, and this task is not an easy one when it comes to deciding which cases of obscure death deserve to be completely investigated. In deciding whether or not an autopsy should be performed in a case of sudden or obscure death the medical examiner should be aware of the possibility that death resulted from unsuspected poisoning. Many poisons act so suddenly or with such complete lack of characteristic signs or symptoms that deaths caused by them are likely to be attributed to natural causes until the true facts are disclosed by autopsy. That cases of this kind are overlooked is indicated by the recent disclosure in Philadelphia and Cincinnati of the prolonged and successful operation of poisoners.

It is difficult to propose, prior to post-mortem examination, any general rules by which to distinguish between the cases of death that should and those that need not, be the subject of autopsy. To exclude the possibility of death by violence it is highly important, however, that the medical examiner be aware that the apparent innocence of a case is often deceptive. He must also be familiar with the commoner forms of sudden or unexpected death as a result of disease.

Sudden death from natural causes may be divided into three categories according to the nature of the fatal seizure and the time that elapses between its onset and death.

INSTANTANEOUS DEATH

In the first category are the so-called instantaneous deaths. The victim may collapse while at work, at play or at rest. In this form of sudden death cardiac standstill occurs simultaneously with collapse. Death in such circumstances may be compared with the stopping of a clock. One moment the mechanism is functioning adequately, and a fraction of a second later all the wheels have stopped. Death in such circumstances is due to cardiac inhibition, and apparently depends on the existence of either a constitutional or an acquired state of neurocirculatory instability. The studies by Weiss and Baker¹ of reflex carotid-sinus syncope

*Presented at a meeting of the Massachusetts Medico-Legal Society, Boston, February 7, 1940.

†Professor of legal medicine, Harvard Medical School.

and by Capps² of reflex pleural syncope illustrate how constitutional predisposition may lead to this type of catastrophe. The stimulus that initiates the fatal cardiac inhibitory reflex may be provided by excitement, fear, anxiety or any other strong emotional disturbance. A minor physical injury or the induction of anesthesia may precipitate collapse. It is quite possible that the so-called "thymico-lymphatic death" of infants and children depends on the existence of a hyperirritable cardioregulatory mechanism.

Although instantaneous death may and occasionally does occur in persons in whom there is no recognizable heart disease, it is seen more frequently in association with cardiovascular disease. The disease need not, however, be of such severity as to be necessarily incompatible with life. Among the various types of heart disease in which instantaneous death is likely to occur, coronary arteriosclerosis, with or without thrombosis, is the commonest. Syphilitic aortitis, especially when the aortic valve or the coronary ostia are involved, is another predisposing cause. Congenital cardiac anomalies, as well as hypertensive, degenerative or inflammatory heart disease, may lower the threshold of irritability to such a degree as to predispose the heart to instantaneous stoppage.

UNEXPECTED SYNCOPE WITH DEEPENING UNCONSCIOUSNESS TERMINATING IN DEATH

In the second category of sudden deaths the fatal seizure is ushered in by sudden and unexpected loss of consciousness, but death does not take place instantaneously. Minutes or even hours may intervene between syncope and death. The commonest cause of this type of sudden death is heart disease, and of the various kinds of heart disease, coronary sclerosis, with or without thrombosis, is pre-eminent. In cases of sudden death due to coronary thrombosis, microscopic examination of the thrombus usually shows that it had begun to form hours or days before it led to interference with cardiac function. Death from coronary arteriosclerosis may occur without thrombosis and with no evidence of recent change to correspond with the dramatic functional changes observed. A cause of sudden heart failure that is commoner than has been heretofore suspected results from occlusion of the lumen of a coronary artery by hemorrhage into an atheromatous plaque. Degenerate intimal plaques frequently show rich capillary vascularization, and it is not unusual for the capillaries to rupture, with the formation of a subendothelial hematoma, which to the naked eye bears a close resemblance to a thrombus.

Any type of developmental, degenerative or in-

flammatory heart disease is likely to predispose to sudden death. More times than not death, although sudden, is by no means unexpected. However, death may occur unexpectedly in degenerative or inflammatory heart disease, because in either, the presence of cardiac disease may be entirely unsuspected. Thus, the myocardial degeneration seen in children who have recently recovered from some infectious disease occasionally results in sudden death. Extreme degrees of myocardial replacement by infiltration of fat may be responsible for unexpected heart failure, usually in persons who are past middle age, obese and of sedentary habits. Severe forms of chronic rheumatic carditis may be found in persons whom no one suspected of having been ill. Aortic stenosis is frequently responsible for the unexpected collapse and death of relatively young adults. Aortic valvulitis of this type is apt to take the form of a monovalvular disease in which the cusps have become adherent so as to form a thick fibrocalcereous diaphragm, in the center of which is situated the greatly reduced valve orifice. Patients with this type of heart disease frequently carry on normally, and then for no apparent reason collapse and die within a few minutes.

Although circulatory failure is the most frequent cause of sudden loss of consciousness terminating in death, this type of seizure may result from any one of several intracranial disturbances independently of heart failure. Of these, hemorrhage, either within or around the brain, deserves first consideration. Most sudden and rapidly fatal intracranial hemorrhages are of three kinds.

The first is ordinary cerebral apoplexy, occurring in persons past middle age as a result of a combination of high blood pressure and degenerative disease of the cerebral arteries. As a rule death does not occur until several hours or even longer after loss of consciousness. In the case of massive hemorrhage in the basal nuclei with rupture into a ventricle, death may occur very soon after the onset of unconsciousness. Almost instantaneous death may follow the rupture of an artery in the pons.

The second type of fatal intracranial hemorrhage is due to bleeding from a congenital miliary aneurysm. Such hemorrhages are usually subarachnoid and occur most commonly in young adults; the fatal attack is usually preceded by a severe headache. It is thought that these aneurysms represent a developmental anomaly. They may be single or multiple, and are usually found at sites of bifurcation of the superficial arteries at the base of the brain.

The third type of cerebral hemorrhage occurs

in a richly vascularized brain tumor. Such brain tumors may occur at any age, and are frequently asymptomatic prior to the occurrence of the fatal hemorrhage.

It is customary to regard a hemorrhage within the substance of the brain as having resulted from natural causes until proved otherwise. Such an assumption is usually justified, but it should be borne in mind that deep cerebral hemorrhage may result from unsuspected head injury. Bleeding may occur at the site of a cerebral contusion days or even weeks after the injury has been sustained. Extensive pathological study may be required to distinguish between traumatic and spontaneous hemorrhages of this type.

Other less common intracranial causes of sudden loss of consciousness followed by death include arterial thrombosis or embolism, meningitis, encephalitis and the sudden development of edema in the vicinity of a tumor or abscess.

Diabetic acidosis, uremia and acute adrenal insufficiency are also occasional causes of sudden death. In diabetic acidosis the evidence as to the cause of death may depend solely on chemical examination of the blood and urine.

RAPIDLY FATAL ILLNESS WITH EARLY PROSTRATION NOT INITIATED BY LOSS OF CONSCIOUSNESS

In the third category of sudden deaths, loss of consciousness is not the first manifestation of the fatal seizure. Disability terminating in death progresses with such great rapidity, however, that in cases of this kind the victim is likely to be found unexpectedly dead in bed. Any of the causes of sudden death previously described may operate in this manner. Certain other conditions, however, occasionally cause sudden death without the fatal illness being ushered in by loss of consciousness.

Infection, particularly in the very young or the very old, is likely to progress with such rapidity that the entire clinical course of the disease may be run within a few hours. Thus, a child thought to have been well at noon may be found dead in its bed in the afternoon as a result of a fulminating infection. It is likely that many of the unexpected deaths of young infants commonly attributed to suffocation or to status thymicolymphaticus are actually due to infection. The inflammatory lesions in such cases are characteristically pulmonary. They may, however, be meningeal or intestinal. The lesions are frequently so inconspicuous as to escape recognition on macroscopic examination. Deaths of the aged are also likely to occur as a result of rapidly progressing infection. It is not unusual for an old person who was not thought to have been ill in the evening to be

found dead in bed the next morning as a result of bronchitis, pneumonia or peritonitis. In such circumstances circulatory failure undoubtedly plays an important role.

Another cause of unexpected prostration progressing rapidly to death is hemorrhage. Death may result either from acute anemia or from interference with the function of some vital organ by the extravasated blood. If the bleeding is external, the cause of the prostration and death is apparent, but often the hemorrhage is concealed. Thus, there may be fatal bleeding into the pleural or peritoneal cavity or into the lumen of the intestine, with no external evidence of blood loss. Aneurysm, tumor, varix, ulcer and ectopic pregnancy are among the commoner causes of a concealed fatal hemorrhage.

Intracranial hemorrhage may result in death from increased intracranial pressure even though the actual amount of bleeding is slight. The escape of less than a pint of blood into the pericardiac sac may be sufficient to cause death from cardiac tamponade. The entrance of a few ounces of blood into the air passages may cause the victim to drown in his own fluid, despite the fact that the actual amount of blood lost is insignificant. Common causes of intrabronchial bleeding include aortic aneurysm, and tumor, abscess and tuberculosis of the lungs.

SUMMARY

Although the foregoing discussion of the causes of sudden death is in no sense complete, it includes some of the more important diseases that commonly predispose to unexpected collapse and death. They do so for one of two principal reasons. The disease may render the circulatory system hyperirritable, so that a minor stimulus or stress causes the latter to fail, or the disease may be suddenly converted from a condition that is compatible with life into one that is incompatible.

From a medical standpoint the chief interest in sudden death lies in the fact that its occurrence is often unnecessarily premature. Death may be the result of an avoidable trespass on the physical or functional reserve of the diseased part. This is particularly true in cases of sudden death from heart failure. If the diseased condition were recognized so that the person so affected could be advised how to live within the limits of his diminished reserve, there would be less likelihood of the commission of fatal physical or emotional excesses.

For the protection of such a patient and of persons who might be injured by him, he should be advised against any undertaking in which his sudden collapse might lead to physical injury to him-

self or others. It is apparent that a person threatened with sudden loss of consciousness should not drive an automobile, operate a public conveyance or otherwise engage in potentially dangerous undertakings.

From a medicolegal standpoint the subject of sudden death is of great importance. On the ability of the medical examiner to recognize the lesions responsible for sudden death from natural causes may depend whether an obscure death leads to a criminal indictment or to no charge, or whether or not it results in a civil action for indemnification. Thus, the difference between a verdict of murder and an acquittal may rest on post mortem evidence.

The difference between double and single indemnity in the settlement of insurance claims or the difference between full workmen's compensation and no compensation is likewise apt to be dependent on evidence obtained at autopsy.

The investigation of the causes of sudden death constitutes a problem of far reaching medical and medicolegal significance.

25 Shattuck Street

REFERENCES

- 1 Weiss S and Baker J P. The carotid sinus reflex in health and disease: its role in the causation of fainting and convulsions. *Medicine* 12:29-354 1933.
- 2 Capps J A. Arterial embolism versus pleural reflex as the cause of pleural shock. *J A M A* 109:852-854 1937.

CANCER OF RECTUM AND SIGMOID

WILLIAM M SHEDDEN, MD*

BOSTON

THE American College of Surgeons¹ has complete records of a total of 25,195 five year cures of proved cancer, of which 3,151 are of the colon and rectum. These figures represent only a fraction of the five year cures that have been obtained, yet in a series of 132 carcinomas of the rectum and sigmoid treated by me, it was noted that over 60 per cent appeared for treatment late in the course of the disease. Study of this group brings home forcibly the fact that most, if not all, of the radical resections in these cases could have been avoided if the tumors had been seen in the stage of pre-cancer, for it is now the opinion of most workers in this field that the adenoma is the precursor of most cancers of the rectum and sigmoid. Sunitz states that 75 per cent of all the carcinomas occurring in the large bowel arise in the descending colon, sigmoid, rectum and rectosigmoid. His statistics show that 65 per cent of all the polyps occurring in the large bowel arise in the descending colon, sigmoid, rectosigmoid and rectum. We must, therefore, be more diligent and painstaking in our search for polypoid adenomas. While it is, of course, important to examine with proctoscope and sigmoidoscope any patient passing blood by rectum, it is even more important to perform these examinations on the patient who presents himself without rectal symptoms.

The evolution of the precancerous lesion as accepted by Dukes,² Daniels³ and others is shown in Figure 1. First, there is hyperplasia of the mucous

membrane, at the onset invisible to the naked eye, next, there appear one or more adenomas. In the second stage the lesions may be scattered over a wide area, the color of which has a deeper tint than the surrounding mucous membrane. These early adenomas manifest themselves as very slight elevations of a small area of mucous membrane, and, as they grow larger, become a deep red.

Another variation, possibly a more advanced stage of the evolution, is a branching, treelike process with an ultimate breaking through of the basement membrane. The cells heap up, the nuclei become hyperchromatic, and there is active mitosis. If one does not present the entire lesion to the pathologist for diagnosis, a small area undergoing malignant change may easily be missed.

With the growth in this early stage, the patient usually presents no signs or symptoms, and it is for this reason that as large a number of patients as possible should submit to a proctosigmoidoscopic examination as part of the physical examination in a routine check up. These growths, I believe, can never be regarded with indifference. They must be destroyed at the earliest possible moment.

There is only one satisfactory method of dealing with an area of hyperplasia or an adenoma in the rectum or sigmoid, and that is by electrodesiccation or cautery via the proctosigmoidoscope. This must, of course, be done thoroughly, but in order to avoid the risk of perforation of the bowel, it is often safer to divide the treatment into several sittings.

*Instructor in surgery, Tufts College Medical School; chief of Tumor Clinic, New England Medical Center.

Aylett⁵ has modified a sigmoidoscope* so that diathermy may be easily employed. With this instrument an excellent view of the neoplasm is obtained, and diathermy with a long electrode can be readily carried out under direct vision. The suction tube, by projecting just beyond the growth, sucks the smoke away from the operation.

Bodkin⁶ has devised a "punch-coagulator" which can perform several functions at one introduction:

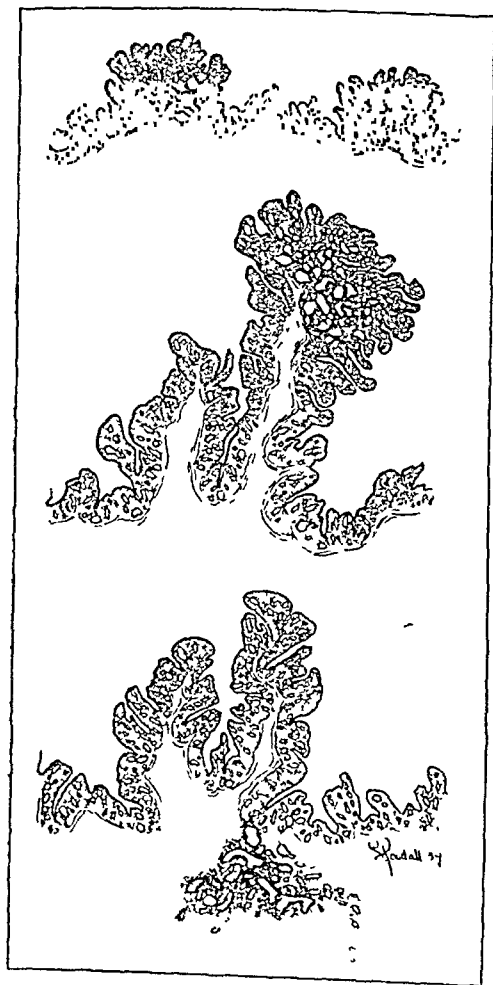


FIGURE 1. *The Development of Rectal or Sigmoidal Cancer (Daniel⁴). (Reproduced by permission of the publisher.)*

punch biopsy, coagulation and aspiration of blood, smoke and detritus. It consists of one steel tube sliding within another, the inner tube sharpened to form a punch, and the outer one moderately pointed to form a coagulating tip. The punching action is completed by squeezing together the halves of a pistol grip. A small spring separates them as pressure is released.

*Made by Vann Brothers, 63 Weymouth Street, London W. 1.

LYMPHATIC DRAINAGE

Palpation of indurated lymph nodes gives little real information. Dukes³ found a 61 per cent error in the clinical diagnosis of carcinomatous nodes. He sectioned over 2000 nodes from 100 cases of rectal cancer, and found metastases in 62 per cent of the cases.

The average distance cephalad between the involved node and the anal margin was 21.25 cm in 24 cases from the above series. The superior hemorrhoidal vessels were ligated 25.4 cm. from the anal verge.

Villemin, Huard and Montagné⁷ suggest that the rectum should be considered as consisting of two parts, each with a different lymphatic drainage. The lower part, the ampullary portion and the

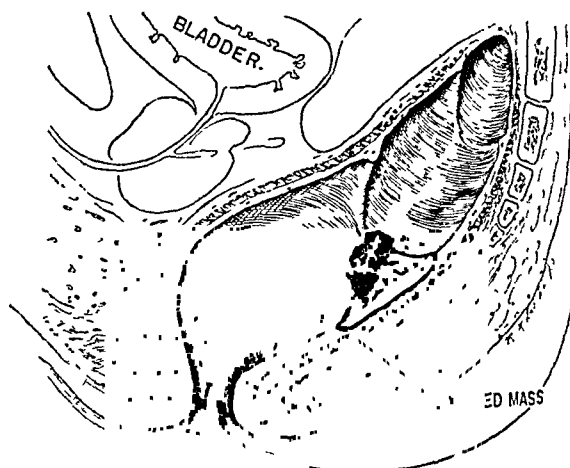


FIGURE 2. *Rectal Adenocarcinoma. A sketch showing the location of the tumor and the excised area.*

anorectal region, drains upward but also laterally and downward, while the upper, that part of the rectum above the lowest valve of Houston, drains only in an upward direction along the superior hemorrhoidal artery.

Gabriel, Dukes and Bussey⁸ consider that downward spread takes place only when the lymphatics above are blocked by growth. The same opinion is held by Gilchrist and David.⁹

Work done by the latter authors indicates that glandular metastasis in cancer of the rectum is not a late phenomenon. Recently I saw in follow-up an apparently healthy patient whose summarized case history illustrates the point just made. He had noticed slight bloody staining of stool twice during the three months before entry six years previously. However, he had observed no rectal pain, tenesmus, mucus or frequent stools. Nevertheless, 7 cm. above the anus was a small.

soft tumor which apparently did not penetrate beneath the submucosa. It was removed widely by electrodesiccation (Figs. 2 and 3). The pathological report read: "A soft mass, measuring 2 by 1 by 1 cm. Diagnosis: adenocarcinoma, Grade II." The



FIGURE 3. Rectal Adenocarcinoma.

Photograph of a section of the tumor that was clinically benign.

patient was persuaded to have a radical resection. The rectum after removal showed no trace of the primary tumor, but was associated with two small pararectal nodes containing metastases (Fig. 4). It is therefore not safe to depend on the criteria of size, soft consistence and mobility in estimating

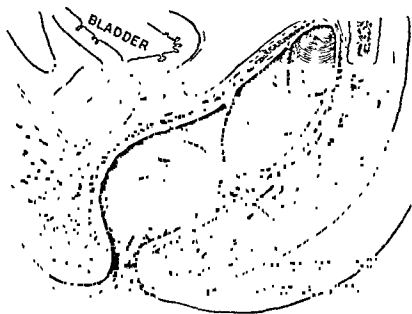


FIGURE 4. Rectal Adenocarcinoma.

A sketch showing the location of the two pararectal lymph nodes containing metastases.

the malignancy of a rectal tumor. This case history also serves to emphasize the point made by Miles¹⁰ and others, that if a diagnosis of adenocarcinoma of the rectum is confirmed, and if the patient's condition warrants it, nothing less than an excision, having as its upper limit a wide mar-

gin of intestine above the growth and including the lymph nodes of the mesosigmoid, is justified.

The series reported by Gilchrist and David⁹ showed 70 per cent involvement of the lymph nodes. Out of 47 specimens removed by abdominoperineal resection, they found 2 in which, as the result of metastases above the growth, a retrograde spread to lymphatic nodes below the growth had occurred. Despite the above, Muir¹¹ advocates a more frequent employment of the anterior resection, the Hartmann operation (Fig. 5), which

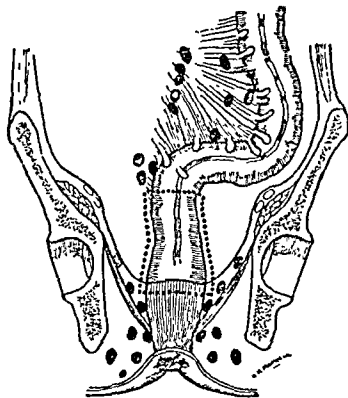


FIGURE 5. Hartmann Operation for Rectal Carcinoma. (Reproduced from Miles's *Carcinoma of the Rectum* [London: Harrison & Sons, Ltd., 1926] by permission of the publisher.)

allows the retention of the rectal stump distal to the level of resection. However, the oldest patient in his series of 9 cases has passed only twenty-eight months since operation. One has already a secondary growth in the rectal stump. In our opinion, the Hartmann operation should be reserved for the rectosigmoid or low-sigmoid growth in the poor-risk patient.

PROGNOSTIC CRITERIA

Grinnell¹² attempts to give a prognosis after grading the tumors, using eight criteria: arrangement of involved lymph nodes, invasiveness, nuclear polarity, number of mitoses, papillary character, extracellular "mucin" secretion, size of nuclei and variation in size of nuclei. The first four only were found to be of value.

Biopsy may not lead to a true grading of the tumor. This is illustrated by a case in our series. The biopsy specimen showed a malignant adenoma, while the tumor in the resected rectum was reported as an adenocarcinoma. Of 74 cases in

Grinnell's series, there were 16 (22 per cent) in which the biopsy specimen was at least one grade less malignant than the tumor was rated. Size is not a reliable criterion of operability; fixation to the sacrum or prostate is as often due to inflammatory reaction as to carcinoma; and mesenteric node involvement can practically never be determined before operation. There is little relation

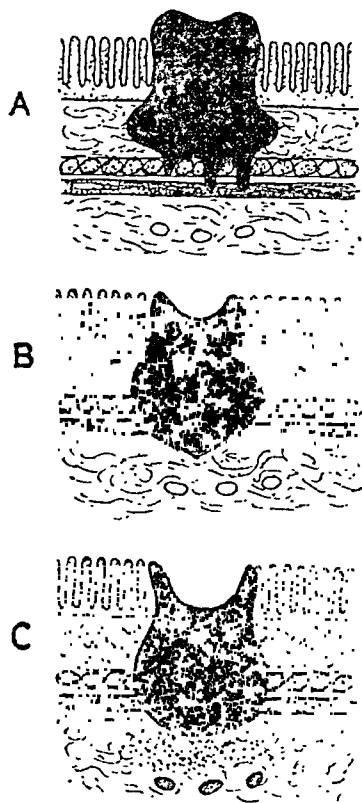


FIGURE 6. Sketch Showing Duke's Classification of Rectal Carcinomas (Grinnell¹²). (Reproduced by permission of the publisher.)

In A, the growth is limited to the wall of the rectum; in B, it has extended to the extrarectal tissues, without involvement of the regional lymph nodes; in C, the lymph nodes are involved.

between the extent of the growth locally and the presence of liver metastases.

Tumors without lymph-node metastases had an incidence of five-year survival two and a half times that of those with node involvement. Tumors classified as projecting or "productive" gave far better five-year results than those classed as infiltrating. Most of the projecting tumors in Grinnell's series were histologically Grade I, and the infiltrating were Grade III.

Dukes³ has commonly found extensive spread within the veins. It may be taken for granted that if this is found, there will be metastases in the liver. He graded a series of carcinomas of the rectum by Broder's method, and checked the re-

sult against the survival rate of these same cases in the first three years as follows: Grade I, 80 per cent; Grade II, 65 per cent; Grade III, 52 per cent; Grade IV, 34 per cent; and colloid, 60 per cent. When these same tumors were graded by Duke's own method,—that is, determination of the extent of the invasion of the surrounding tissues,—it was found that the survival rate on a five-year basis showed 93 per cent in Group A (less than 10 per cent of this group), 65 per cent in Group B and 23 per cent in Group C. Duke classifies carcinoma of the rectum according to the proved depth of spread (Fig. 6). The Group A cases are recognized as those in which the cancer is confined to the rectal wall; that is, the growth has invaded only the submucous or muscular coats; Group B cases are those in which the growth has extended to extrarectal tissues but in which there are no metastases in the regional lymph nodes; Group C cases are those with metastases in the regional lymph nodes. When the Group A cases were studied, it was found that 80 per cent had bleeding as the commonest symptom. Further, it is to be noted that the percentage of Group A cases varied with the social status. Duke showed that there were almost twice as many of these cases among private patients as among "clinic" patients.

Several explanations have been suggested for the higher incidence of advanced cancer in the second group: failure to note symptoms or recognize their importance—it is amazing to see how many of the "clinic" group know only one disease, "piles"—and economic pressure. Many wage earners postpone examination for fear that the discovery of some serious condition may cause the loss of wages and employment. Another common source of error and serious delay is the high incidence of a double rectal condition. For instance, large, prolapsed hemorrhoids are often seen in conjunction with a carcinoma of the rectum; a benign adenoma or papilloma may be present coincidentally with a carcinoma at a higher level. The patient with a discharging anal fistula may also have a rectal cancer. Two carcinomas of the rectum may be present in the same patient, or a carcinoma of the rectum with a second carcinoma of the pelvic colon may occur in as high as 8 per cent of operated cases.

EARLY DIAGNOSIS OF CARCINOMA OF THE RECTUM AND SIGMOID

Over 90 per cent of rectal cancers can be felt by the examining finger. I except a small group high in the rectosigmoid, which should be visualized with the sigmoidoscope. For a digital examination, it is desirable to have the patient in the right

lateral, or occasionally the squatting, position. In any large series, a fifth of the cases of cancer of the rectum will be found to have been operated on for hemorrhoids within the period of their symptoms. The diagnosis of hemorrhoids alone should not be made without digital examination and proctosigmoidoscopy. As regards the growths of the sigmoid, it is to be hoped that at some time in the near future the cost of the barium enema will be brought low enough so that it will be employed more frequently, both as a check up in the case

year age groups, would well repay the trouble and organization required by the detection of early rectal cancers as well as their precursors, adenomas and papillomas. However, schemes for periodic medical examinations will fail if the public is not encouraged to report all rectal symptoms, and if physicians do not insist on the necessity for a rectal examination no matter what may be the coincident diagnosis. It must be remembered, moreover, that cancer also appears in the younger age groups. Bacon and Sealy¹³ report the case of

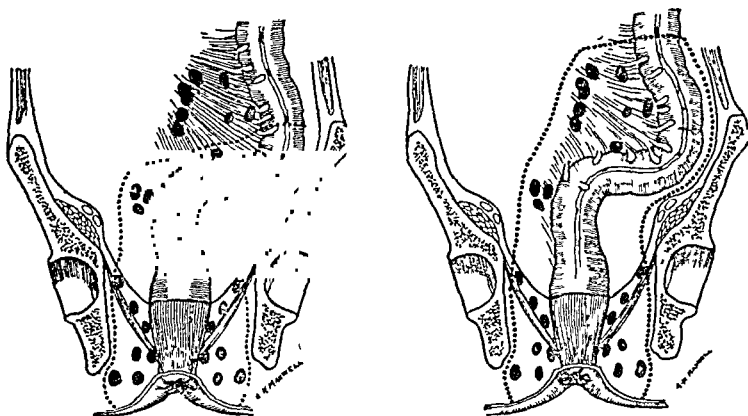


FIGURE 7 Operations for Rectal Cancer (Reproduced from Miles's *Carcinoma of the Rectum* [London: Harrison & Sons, Ltd., 1926], by permission of the publisher.)

The sketch on the left shows limited excision of the mesentery, that on the right radical excision as in the Miles operation.

with symptoms, and as part of a routine periodic physical examination. It is only in this way that a large number of Duke's Grade A cancers will be discovered.

During the last few years, I have had under my care 3 patients with rectal growths who had no bowel symptoms whatsoever. The first was an old man with an arthritis of the right knee. Routine digital examination by his physician disclosed a rectal growth 15 cm. in diameter, which proved to be cancer. The second was a woman who complained to her family physician of a backache. X-ray films of the back were negative. Routine digital examination revealed a tiny cancer of the rectum. The third entered a clinic for treatment of a pilonidal sinus. A digital examination revealed a rectal cancer less than 1 cm. in diameter. The credit for these diagnoses goes entirely to the conscientious physicians who made these rectal examinations.

The semiannual examination of any large group of adults, particularly in the fifty year to seventy

a boy of four with a carcinoma of the rectum arising from a large polyp. These authors collected from the literature 123 authentic cases of malignancy of the anus, rectum and sigmoid below the age of twenty. Abdominal pain, rather than bleeding or rectal tenesmus, is the striking symptom in these young people.

It is perhaps unnecessary to stress here that if a biopsy is taken, a negative report has no more significance than a negative barium enema. It means merely that that particular piece of tissue, or that particular column of barium, has not revealed a growth. Moreover, although often necessary in the diagnosis of neoplasms of the sigmoid and rectosigmoid, x-ray examination plays no useful part in the diagnosis of cancer of the rectum.

TREATMENT OF CARCINOMA

Lockhart-Mummery¹⁴ in 1935 reported 398 cases of cancer of the rectum treated by colostomy and perineal resection, with an overall mortality of only 4.5 per cent in patients under 10 per

cent in hospital cases. During the same period, the combined abdominoperineal operation in his hands showed a mortality of 20 per cent. One hundred and forty-two (52.5 per cent) of his patients surviving operation lived for five or more years. His figures for the combined operation showed only 28 per cent five-year cures.

Contrary to an apparently widespread belief, Lockhart-Mummery neither advocates nor employs perineal excision to the exclusion of all other procedures. He states that his operative procedure is suitable in any case in which the growth is at the anus or anywhere in the rectum proper.

Despite Lockhart-Mummery's results, the Miles¹⁰ abdominoperineal resection of the rectum for cancer (Fig. 7) is enjoying ever-increasing popularity. Rankin,¹⁵ Jones¹⁶ and many others employ it in over 75 per cent of their rectal resections. Jones recently reported 151 cases with 52 per cent alive and well at the end of five years.

The major objection which has been raised to the one-stage combined abdominoperineal method is its high primary mortality. That this mortality is not unduly great is emphasized by three series of cases recently reported. Rankin reports a series of 75 one-stage operations with an operative mortality of 6.6 per cent. Jones recorded a series of 300 one-stage combined operations, with a mortality of 9.2 per cent and an operability rate of 64 per cent. He has utilized this procedure in over 90 per cent of resectable tumors. Scarborough¹⁷ reports 66 one-stage abdominoperineal resections, with an operative mortality of 9.1 per cent and an operability rate of 76 per cent. In Scarborough's series, previous treatment without correct diagnosis was given in 27 cases (41 per cent).

Operability and mortality are usually closely allied. The acceptance of the wide dissection of the lymph nodes affects the mortality and end results.

TABLE 1. *Hospital and Operative Mortality Rates in All Cases of Cancer of the Rectum.*

Cases treated	132
Hospital deaths	11 (8 per cent)
Cases resected	100 (76 per cent operability)
Operative deaths	11 (11 per cent)

Table 1 shows the mortality and operability rates in my cases. The end-results in the 100 resected cases are shown in Table 2.

The trend of the latest 50 resected cases in this group is interesting: although the operability rose from 76 to 79 per cent, the mortality dropped from 11 to 4 per cent. In this group there were forty-one (82 per cent) one-stage operations, and nine two-stage operations.

The Miles operation, of course, entails a colostomy. There is constant pressure, both by the patient and the family physician, to have a local nonmutilating operation performed by which the sphincter is preserved. The demand is the more insistent if the lesion is small, but it is the opinion of most surgeons experienced in dealing with this disease that, in general, although the malig-

TABLE 2. *End-Results in 100 Resected Cases of Cancer of the Rectum.*

NO. OF YEARS OF FOLLOW-UP	NO. OF CASES	NO. OF PATIENTS LIVING AND WELL
14	1	1
8	2	2
7	1	1
6	6	4
5	3	2
4	8	8
3	14	8
2	13	6
1	18	9
Less than 1	32	10
No recent follow-up	2	—
Totals	100	51

nant lesion be small, the surgery must be as aggressive as if it were large. Moreover, it has been my experience that the chief and most vociferous objectors to colostomy among patients are those who do not have a colostomy and do not need it to remain alive. As Rankin¹⁵ puts it, "in the main the surgical world rarely dissents from the dictum that a colostomy is a necessary part of a radical curative operation for cancer of the rectum." It is unfortunately true that the general practitioner is far from being universally convinced of the necessity or desirability of this step. Five-year cures from sphincter-saving operations number approximately 33 per cent, whereas, as has been shown above, the more radical one-stage combined abdominoperineal procedure may show a rate of 63 per cent.

To avoid the mortality of the abdominoperineal or perineoabdominal excision of the rectum, Lynch¹⁸ urges that both these technics give way to a perineal excision of the rectum without the accompanying colostomy. It seems to me that there are two important objections to Lynch's technic: first, that it results in a sphincterless perineal fistula; and second, that it can never remove as much of the sigmoid mesentery as is possible with the Miles technic (Fig. 7), and that there will thus be a relatively high percentage of recurrence. At any rate, we shall have to reserve judgment concerning the report of Lynch,¹⁹ inasmuch as it appeared in 1937, three years ago, at which time but 15 cases had been operated on in this manner, and so cannot be compared with any series of abdominoperineal or perineoabdominal operations as regards five-year end results.

It is my opinion that perineal resection is best reserved for that group of patients who, because of old age or chronic constitutional disease, are considered poor surgical risks.

Dixon²⁰ advocates the reconsideration of the plan of segmental resection of the pelvic portion of the colon. Although he employs a relatively safe operation—that is, one performed in stages and with a temporary colostomy—this procedure employed at this bowel level of the sigmoid will, in my opinion, inevitably result in an increased number of recurrences; for, as Miles¹⁰ has shown, the spread of malignancy in this region is occasionally downward, and thus dangerous tissues are left behind.

RADIUM TREATMENT

Most surgeons experienced in the treatment of cancer of the rectum agree that the only cases in which the use of radium is justifiable are those in which a small, early tumor cannot be operated on because of advanced age or concomitant disease. The number of cures will be increased if one employs electrocoagulation of the tumor in addition to radium treatment. I have seen a few of these small carcinomas disappear and the patient remain cured. It has been suggested by Lynch¹⁸ and others that removal of a primary growth may cause the disappearance of secondary lesions in persons of slight susceptibility to cancer. This, it seems to us, has yet to be proved. Lockhart-Mummery¹⁴ advocates the use of radium with squamous carcinoma of the anus. However, this form of treatment involves a rather painful and tedious therapy and one which, in my opinion, does not give the patient the best chance for cure.

Binkley²¹ reports 34 cases of adenocarcinoma following radiation therapy. He employed roentgen therapy at 200 kv., followed by the use of gold seeds of radon totaling 1000 to 5000 millicurie hours. Nine patients (26 per cent) were clinically free of disease five to ten years after treatment.

URINARY COMPLICATIONS

Kickham and Bruce,²² in an analysis of 440 carcinomas of the rectum at the Pondville State Hospital, found frequent and painful urination common. In 96 cases there was adherence to the prostate, and of these, 50 per cent had bladder symptoms.

There was post-mortem examination in 132 cases. Eighty-eight of these, in which no surgical treatment had been directed to the extirpation of the rectal lesion, revealed that 48 per cent had obstruction to the urinary tract secondary to occlusion by malignant disease. Thirty per cent of

men and 37 per cent of women had urinary symptoms, but it must be remembered that there is a high percentage of very advanced cancer in this Pondville group. The authors advise routine vasectomy as a prophylactic against epididymitis. However, in my series, which contained 94 men, this was found necessary in but 1 case. In this case, the patient had an inoperable carcinoma, and was in great pain. Subtheal alcohol injection resulted in complete urinary retention, necessitating a permanent inlying catheter. In my experience epididymitis has been encountered rarely, and then only in its mildest form.

Jones¹⁶ does not put his patients on catheter drainage postoperatively, but has them catheterized every eight hours, for, he says, 30 per cent void spontaneously. Graves and Buddington²³ came, however, to the conclusion that the most satisfactory technic is the employment of a retention catheter, usually No. 16 Fr. and double-eyed, until the patient first leaves his bed after the rectal resection—that is, a period of eight to fourteen days. During this time the catheter is disturbed as little as possible, and is not changed or even irrigated unless there is reason to believe that it is not draining freely.

In a study of 190 men with carcinoma of the rectum, Engel²⁴ found that 5 per cent had obstruction of the bladder neck. He used the cystometrogram to assist in the differentiation of this condition and a neurogenic cause of urinary retention. He believes that the treatment of choice is transurethral resection. It is recognized, however, that both conditions may occur simultaneously with carcinoma of the rectum. These were two distinct cancers. In a few cases, one may expect extension of the carcinoma of the rectum around the neck of the bladder to produce symptoms of urinary obstruction.

SUMMARY AND CONCLUSIONS

The elimination of tumors of the rectum in the stage of precancer will markedly reduce the number of radical resections necessary for the treatment of carcinoma in this region.

Lymph-node metastasis is not always a late phenomenon with cancer of the rectum and sigmoid.

The retention of the rectal stump in resections of the rectum or rectosigmoid for cancer subjects the patient to the risk of recurrence in the stump in a considerable number of cases.

Biopsy may not indicate the true pathological grading of the tumor; a negative biopsy does not rule out cancer.

Dukes's method of grading cancer of the rectum is a satisfactory supplement to that of Broders.

In order that more early cancers may be discovered patients must be examined with the finger, sigmoidoscope and barium enema *before symptoms develop*.

The Miles operation is still the treatment of choice for cancer of the rectum. The mortality has been brought to a relatively low figure, and the cures may be over 50 per cent.

270 Commonwealth Avenue

REFERENCES

1. Report of the Committee on Treatment of Malignant Disease. *Year Book*. 978 pp. Chicago: American College of Surgeons, 1938. P. 21.
2. Saint, J. E.: cited by Lahey, F. H.: Carcinoma of colon and rectum: deductions from eight hundred operations. *Ann. Surg.* 110:1-13, 1939.
3. Dukes, C. E.: Examination and classification of tumors of rectum and colon. *Am. J. Surg.* 46:181-185, 1939.
4. Daniels, E. A.: Precancerous lesion of rectum and sigmoid. *Internat. Clin.* 2:140-151, 1939.
5. Aylett, S. O.: Miles's abdomino-perineal operation: treatment before and after. *Lancet* 2:1516-1518, 1938.
6. Bodkin, L. G.: Punch-coagulator for rectal carcinomas. *M. Times, New York* 67:368, 1939.
7. Villemain, F.; Huard, P., and Montagné, M.: Recherches anatomiques sur les lymphatiques du rectum et de l'anus. *Rev. de chir.* 63:39-80, 1925.
8. Gabriel, W. B.; Dukes, C., and Bussey, H. J. R.: Lymphatic spread in cancer of rectum. *Brit. J. Surg.* 23:395-413, 1935.
9. Gilchrist, R. K., and David, V. C.: Lymphatic spread of carcinoma of the rectum. *Ann. Surg.* 108:621-642, 1938.
10. Miles, W. E.: Problem of surgical treatment of cancer of rectum. *Am. J. Surg.* 46:26-39, 1939.
11. Muir, E. G.: Abdominal resection for rectal cancer. *Lancet* 1:1094-1097, 1939.
12. Grinnell, R. S.: Grading and prognosis of carcinoma of colon and rectum. *Ann. Surg.* 109:500-533, 1939.
13. Bacon, H. E., and Sealy, W. B.: Malignancy of anus, rectum and sigmoid colon in the young: with report of case at four and a half years. *Am. J. Surg.* 45:339-347, 1939.
14. Lockhart-Mummery, J. P.: Causes of haemorrhage from rectum. *Brit. M. J.* 1:997-1000, 1938.
15. Rankin, F. W.: Modern surgical treatment of cancer of rectum and rectosigmoid. *West Virginia M. J.* 35:201-206, 1939.
16. Jones, T. E.: Operability and types of surgery in cancer of the rectum. *Am. J. Surg.* 46:45-47, 1939.
17. Scarborough, R. A.: One-stage abdominoperineal resection for carcinoma of rectum: report of sixty-six cases. *West. J. Surg.* 47:357-363, 1939.
18. Lynch, J. M., and Hamilton, G. J.: Facts and fallacies in treatment of rectal cancer. *Am. J. Surg.* 43:39-44, 1939.
19. Lynch, J., and Hamilton, G. J.: Lynch's simplification of perineal excision of the rectum. *Am. J. Surg.* 36:618, 1937.
20. Dixon, C. F.: Surgical removal of lesions occurring in sigmoid and rectosigmoid. *Am. J. Surg.* 46:12-17, 1939.
21. Binkley, G. E.: Selective surgery in operable rectal cancer. *Am. J. Surg.* 43:51-54, 1939.
22. Kickham, C. J. E., and Bruce, N. H.: Urological complications in malignant disease of the rectum. *J. Urol.* 41:541-556, 1939.
23. Graves, R. C., and Buddington, W. T.: cited by Shedden, W. M.: Carcinoma of the rectum and sigmoid. *Am. J. Surg.* N.S. 44:483-522, 1939.
24. Engel, W. J.: Bladder neck obstruction associated with carcinoma of the rectum. *S. Clin. North America* 19:1195-1203, 1939.

SOME PROPOSED CHANGES IN THE MASSACHUSETTS LAW AS IT RELATES TO MEDICAL PRACTICE

STEPHEN RUSHMORE, M.D.*

BOSTON

FROM time to time changes in the statutes concerning the practice of medicine in Massachusetts are suggested, and some of these suggestions are presented at the office of the Board of Registration in Medicine. Often they are proposed in connection with complaints, occasionally because someone wants something for which the law does not make specific provision, occasionally because the thing wanted is contrary to the statute. The various reactions can be comprehended in the words, "There ought to be a law about it."

For the purpose of informing the medical profession what kind of thing is receiving attention, a number of the proposals have been brought together and arranged with some slight regard for content. The list is not exhaustive, and must not be thought to indicate the changes that any known person or group would regard favorably. Some of the matters may seem trivial; others are of considerable importance. It is hoped that the publication of the suggestions will lead to discussion and better understanding of the situation and in some cases to action. It is, of course, impossible to present with the listing adequate discussion of the many questions involved.

*Secretary, Massachusetts Board of Registration in Medicine.

Definition of the Practice of Medicine

If the writing of statutes were in accord with strict logic, the Medical Practice Act would begin, like some other acts, with a statement of what the act is about. If it is to regulate the practice of medicine, the practice should be defined, and the nature and scope of the regulation, and the machinery therefor, should be set forth.

In favor of attempting a definition is the consideration that this procedure is logical and that until the definition is placed in the statute, the law-enforcing agencies will remain in doubt on several points. Against definition is the alleged impossibility of securing clarity and precision. It is said to be impossible to put in just what one wants and to leave out just what one does not want.

Composition of the Board of Registration in Medicine

The composition of the Board should be determined by the functions that the Board is to perform. These are briefly two: to license and to unlicense. Up until the law of 1936, which has not yet become effective, the most important condition to be met by the applicant for registration was passing an examination, characterized by the

statute as "sufficiently thorough to test the applicant's fitness to practice medicine" Since graduates of any legally chartered medical school—and there is nothing in the statute to exclude a graduate of a legally chartered diploma mill—must be admitted to examination, this test has become substantially *the* test.

What statutory qualification has the Board for performing the function of examining applicants? Such qualification is referred to, for the law reads "No member of said board shall belong to the faculty of any medical college or university" Now, it is not true that once a member of a medical-school faculty, always a member, but practically the selection of board members is limited to a group in the profession less fitted by training and experience to perform the more important of the two functions than are those who are excluded

Board of the Healing Arts

As specialization has developed and become more articulate, the number of boards of registration has been increased, and each group of practitioners has sought independence and autonomy, often losing sight of the prime consideration in creating a board, namely, increased protection for the public It has been suggested, therefore, that there be created a Board of the Healing Arts, which would not interfere with the independence of the practitioners but would unify the administration and the protective procedures

Basic Science Law

As boards for the various subdivisions of the healing art have increased in number, it has been noted that some of these divisions are practically based on different therapeutic procedures, that is, methods of treatment, using the term "treatment" in its commonly restricted sense Therefore it has been suggested, and in some states enacted, that all practitioners of the healing art shall show themselves as qualified in the basic sciences underlying the practice of medicine, no matter in what restricted field they practice. There are always exemptions for certain groups, and although some observers assert that the law has been of great assistance in dealing with cults, others think that it is not an adequate means of handling this problem

Requirement of Internship

With the increasing realization of the importance of the internship as a part of the education of the physician, there has been a tendency on the part of medical schools to require an internship before conferring the degree, and on the part of

state boards to make the same requirement for admission to examination for registration

Repeating Examinations Indefinitely

Under the present statute, candidates once admitted to examination must be admitted indefinitely, regardless of the number of failures, on payment of the required fee. It has been suggested that the number of readmissions without intercurrent formal medical education be limited. The objection to this proposal is that no educational institution will accept these applicants for further training.

Registration of Medical Students

Under the statute, medical students are registered at the end of the second year as "assistants in medicine." Abuses have been brought to the attention of the Board, in connection with non-approved schools, for which the present law provides no remedy. Perhaps the elimination of non-approved schools will meet this situation, but the wording of the statute should be clarified

Interns' Licenses Limited to Three Years

The widening of the scope of the work of interns, with the development of graduate assistantships and of residencies has brought about a situation not contemplated by the original act that licensed interns. It is quite generally agreed that more discrimination should be exercised in the granting of these licenses, but the difficulty has been and still is at what point to draw the line The protection of the public is the first consideration, and the duties of the resident require a maturity of judgment and an exercise of discretion closer to those of the qualified physician than to those of the mere intern who may be a student in his fourth year Additional requirement is therefore reasonable in principle, and the three year limit is not unreasonable in practice.

An objection which may have force on account of possible discrimination against Massachusetts hospitals is that, if full registration is required, it is of no value in securing registration in some other state, and many of the residents will go to other states for practice It is not quite true that registration in Massachusetts is of no value in securing registration in another state, because in some states there is registration by endorsement of credentials; but although the number of residents affected is small because so many of them are diplomates of the National Board of Medical Examiners, the objection is sound from the point of view of the applicant and of the hospital. At the present time the term of the license is at the discretion of the Board

Temporary License

In some states provision is made for a temporary license, valid until the next examination by the Board. It has been suggested that Massachusetts make a change in its statute to meet this situation.

Endorsement of Credentials

Registration by endorsement of credentials has already been referred to, as applicable to physicians registered in Massachusetts. Under these conditions, the other state discriminates among registrants in Massachusetts and may reject all, or only those who do not satisfy the requirements for admission to examination, for example, those who are graduates of nonapproved schools. When the Approving Authority becomes effective, it may be appropriate to make a change in the Massachusetts law. With the law as it is, the Massachusetts license to practice has become a kind of joke among the other states.

Annual Registration of Physicians

The argument in favor of the annual registration of physicians is that the State and the public should know from the records of the State itself, and not from those of some private organization, what persons are registered by the State and are practicing and where they are practicing. At present no provision has been made for an accurate and up-to-date list of registered physicians. Against the proposal to secure such a list there can be no argument, and the only argument against the proposals of past years is that the doctors should not be taxed for the purpose of keeping the register accurate and up-to-date.

License to Practice Surgery

Some of the more dramatic abuses that come to the attention of the Board are in the practice of surgery, usually by unqualified persons. It is suggested that surgery be practiced only by persons specially licensed therefor. The practical difficulties are considerable.

Licensing of All Hospitals

It has been suggested that all hospitals be licensed under conditions that would ensure adequate equipment and medical and nursing care.

Licensing of Hospitals for Surgery

It has been suggested that no surgery, except in emergency, be permitted outside of properly equipped and licensed hospitals.

Licensing of Nursing and Convalescent Homes

The studies of these institutions which have been made in recent years suggest that more control over them would increase protection for the inmates.

As new statutes are introduced and old statutes are modified, it is easy to omit the consideration of some details, so that occasionally contradictions occur, and often clarification is needed. Several proposed changes of this character are noted below.

Dentistry

Since the practice of a specialty, as dentistry or optometry, is authorized by the statute, there is usually a prohibition against practice by persons not specifically authorized, which prohibition is not always worded felicitously. The dental law does not correspond, as it of course should, with the actual practices carried on by common agreement by the medical and dental professions.

Optometry

Under the present optometry law, as interpreted by the Supreme Court of Massachusetts, a registered physician who practices optometry is not under the jurisdiction of either the Board of Registration in Medicine or the Board of Registration in Optometry. This situation demands attention, since the only control over such a physician seems to be the criminal law.

Qualifications for Signing Commitment Papers

Under a recent ruling by the Attorney General, an intern registered for three years meets the requirement of the statute as to registration and practice for qualification for committing allegedly insane persons for institutional care. Hitherto the Board has interpreted the statute as referring to a person registered for three years as a qualified physician. Apparently this peculiarity is due to a change in one part of the statute, and a failure to make all other related sections consonant therewith.

Chiropody

The changes needed here may be called merely clerical. When a separate board was created for chiropody, not all references to chiropody in the medical practice act were removed.

Copy of the Medical Practice Act

It might prove helpful, and would certainly be desirable, to give each registrant, with his certifi-

cate of registration, a copy of the law under which he is to practice medicine. This is done by some boards, but it is not authorized by statute in Massachusetts.

Uniform Narcotic Law

In spite of the variations in the practice of medicine among the states, there is no reason why the laws governing the control of the use of narcotics should not be uniform, some progress has been made in this direction, but not with the participation of Massachusetts. The advantage of uniform laws, if they are just and effective, is obvious.

Expert Medical Testimony in Court

This is a problem the solution of which has been given up in despair by some persons. It belongs to law as well as to medicine, and can probably be solved by intelligent co-operation. Whether statutory enactment is necessary is not yet clear, but it has been advocated.

Physiotherapy

That there should be additional control of the practice of physiotherapy is generally acknowledged, but opinion varies as to the best method. Licensure is an obvious remedy for well known abuses, but has not proved uniformly satisfactory where adopted. Certainly this matter demands attention.

Criminal Abortions

In detecting criminal abortionists the police have found a somewhat disconcerting lack of co-operation by physicians and by hospitals. The difficulty lies in part in the practical impossibility in many cases, of determining any facts except that the patient has had a miscarriage and is septic, and of course the first duty of the physician is to assist the patient in recovery, if possible. The statute requires the reporting to the police of every wound produced by a firearm which comes to the attention of the physician for treatment, but even the most enthusiastic advocate of the reporting of abortions recognizes that the analogy is not perfect. Perhaps reporting all septic abortions would be a step in the right direction.

Certificate of Deceased Physician

It has been suggested that the certificate of registration of a deceased physician be returned to the board for cancellation, and thereafter be destroyed, or, if desired by the family of the physician, returned to them.

520 Commonwealth Avenue

CLINICAL NOTE

ACQUIRED HYPERSENSITIVITY TO SULFAPYRIDINE AND SULFAMETHYLTHIAZOLE*

ARNOLD DAVIDSON, M.D.,† AND
JESSE G M BULLOWA, M.D.‡

NEW YORK CITY

SULFAPYRIDINE is widely used in the chemotherapy of gonorrhea and pneumonia. Sulfamethylthiazole, recently introduced, is closely related to sulfapyridine and has been used only in investigative work.

True acquired hypersensitivity to sulfanilamide has been described by Salvin,¹ Schonberg,² Goodman and Levy,³ Frank,⁴ Schwentker and Gelman,⁵ Mainzer,⁶ Schlesinger and Mitchell,⁷ Tedder⁸ and Garvin.⁹ In each case reported a reaction, usually chills, fever and a rash, occurred during treatment after the patient had already received a substantial amount of the drug, and was reproducible later by the administration of a small amount of sulfanilamide. Gallagher¹⁰ describes a case in which there was a lapse of two years between the original treatment and the readministration. In a case described by Steven¹¹ there were chills and fever but no rash. Thompson¹² describes 2 cases of induced hypersensitivity to sulfapyridine, in both of which the patients developed systemic reactions, fever and skin lesions—in the first case morbilliform and in the other a generalized macular roseola—after they had been receiving the drug for eight and ten days, respectively. The reaction disappeared when the drug was discontinued, but in each case returned in an acute form when the patients were given 1 gm of sulfapyridine eighteen and five days later, respectively. Erskine¹³ describes a similar case in which a generalized erythema developed after fourteen days of treatment with sulfapyridine and was reproduced twenty five days later by 0.5 gm of the drug. He also describes a patient who had no reaction originally but who developed a scarlatiniform eruption on the readministration of sulfapyridine twelve days later. Similar induced hypersensitive reactions to closely related drugs have been described. Love and Simon¹⁴ report a case in which a fixed

*From the Medical Service, Harlem Hospital, Department of Hospitals, New York City.

This study was aided by a grant from the L. Bauer Pneumonia Research Fund of New York University College of Medicine and received additional financial support from the Metropolitan Life Insurance Company and from Mrs. Bernard M. Paruch, Mr. Bernard M. Paruch, Jr., Miss Belle M. Paruch and Mrs. H. Robert Sami, Jr.

†L. Bauer Research Fellow in Pneumonia, New York University College of Medicine.

‡Clinical Professor of Medicine, New York University College of Medicine, consulting physician, Harlem Hospital.

eruption and stomatitis occurring during treatment with sulfanilamide was reproduced by a small dose of neoprontosil. Erskine¹³ describes a case that was sensitized to sulfanilamide by therapy with sulfapyridine.

We report the occurrence of acquired hypersensitivity to sulfapyridine and sulfamethylthiazole after treatment with sulfapyridine.

CASE REPORT

H. M., a 34-year-old Negro, was admitted to the Harlem Hospital on January 19, 1940, with a history of pain in the left chest, worse on deep inspiration, which had been present for 2 days. Cough, productive of rusty sputum, had existed for 1 day. Except for "pleurisy" about 1 month previously the past history was noncontributory. There was no history of allergy or of drug sensitivity.

Physical examination on admission revealed a well-developed and well-nourished, acutely ill Negro. The temperature was 104°F., the respirations 40 and the pulse 110. There was dullness over the lower half of the left chest posteriorly, with diminished breath sounds and many crepitant rales in that area, extending into the axilla. The admission diagnosis of lobar pneumonia, left lower lobe, was confirmed by radiographic examination.

No pneumococci were found on direct examination of the sputum or on mouse inoculation, and the patient was given sodium sulfapyridine by mouth on the day after admission. After he had received 12 gm. the temperature fell to 100°F., and the sodium sulfapyridine was discontinued. On January 23, because the temperature had continued between 100 and 101°F., sodium sulfapyridine by mouth was again given, 1 gm. being administered every 4 hours day and night until January 27, when it was discontinued because a rise in temperature to 103°F. on that day was thought to be due to the drug. The temperature remained between 100 and 101°F. without apparent cause other than the resolving pneumonia. X-ray examination on January 29 showed no evidence of fluid. On February 2 the patient complained of slight pain in the right popliteal space and the possibility of a thrombophlebitis was entertained; however, there was no other evidence to support such a diagnosis.

On February 7, 11 days after the sulfapyridine had been discontinued, the patient received 5 gm. of sulfamethylthiazole by mouth. This was followed in 3 hours by a very mild generalized itching, a generalized erythematous eruption starting on the face and chest, a marked conjunctival injection, a feeling of coldness without an actual chill and a rise in temperature to 105.4°F., 7½ hours after the ingestion of the drug. By the next morning the entire reaction had subsided, and the temperature had dropped to 99°F. This acute febrile reaction apparently had the effect of nonspecific fever therapy, since thereafter the temperature remained below 100°F.

On February 15 the patient was given 0.5 gm. of sulfamethylthiazole orally at 10:30 a.m. At 1:00 p.m. the hypersensitive reaction was again noted: the patient complained of generalized itching; he had a generalized erythema, marked conjunctival injection and chilly sensations. The temperature then began to rise, reaching 102.8°F. at 7:00 p.m. (Fig. 1). The reaction and fever had disappeared by the next morning.

On February 17 the patient had excreted all the sulfamethylthiazole and was given 0.5 gm. of sulfapyridine by mouth at 10:30 a.m. At 1:00 p.m. his temperature was rising and he had a marked itching, a diffuse erythema,

marked conjunctival injection and chilly sensations. The temperature rose to 103.8°F. at 6:00 p.m. The next morning it was 99°F., and the reaction had subsided. This reaction had been the severest one that the patient had experienced, and although his temperature was almost normal and the manifestations of sensitivity had disappeared the patient stated that he felt as if he had been "beaten up."

On February 20 the patient was given 5 gr. of sulfanilamide by mouth but showed no reaction and no rise in temperature.

Patch tests with sulfapyridine, sulfamethylthiazole and sulfanilamide were negative. Blood-cell counts taken after the reactions had subsided revealed nothing significant—no evidence of hemolysis, eosinophilia or agranulocytosis. The urine on two occasions showed white blood cells and clumps of pus, but this condition cleared up and the urine

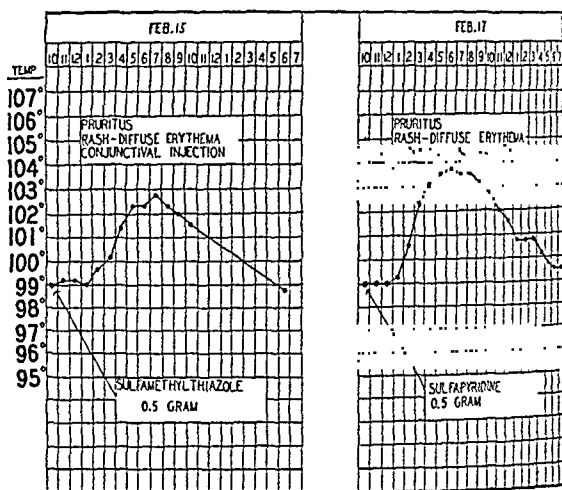


FIGURE 1. Reactions to Small Doses of Sulfamethylthiazole and Sulfapyridine in a Patient Sensitized by Sulfapyridine.

was negative on the day before the patient left the hospital. The blood chemical findings were normal, and a blood Kahn test was negative.

On February 25 the patient left the hospital fully recovered.

COMMENT

This patient was apparently sensitized by his treatment with sulfapyridine to both sulfapyridine and its closely related derivative, sulfamethylthiazole. When he first received sulfapyridine and when it was readministered two days later, he had no untoward reactions. The drug was discontinued four days after it had been readministered because of an unexplained rise in temperature. There was at this time no skin lesion. The acute reactions exhibited subsequently to 5 gm. and then to 0.5 gm. of sulfamethylthiazole and to 0.5 gm. of sulfapyridine were identical, and closely resembled similar hypersensitive reactions described for sulfanilamide and sulfapyridine by other observers. In this case the reaction consisted of a scarlatiniform eruption, pruritus, fever, chilly sensations and conjunctival injection. It is interesting to

note that although the patient became hypersensitive to sulfapyridine and to the closely related sulfamethylthiazole, he was apparently not sensitized to sulfanilamide.

Sulfapyridine is widely used, and it should be recognized that there may occur a hypersensitive reaction such as that described when sulfapyridine and closely related compounds are administered after having been discontinued.

REFERENCES

1. Salvin, M.: Hypersensitivity to sulfanilamide. *J. A. M. A.* 109:1038, 1937.
2. Schonberg, I. L.: Purpuric and scarlatiniform eruption following sulfanilamide. *J. A. M. A.* 109:1035, 1937.

3. Goodman, M. H., and Levy, C. S.: Development of cutaneous eruption (toxicodermatosis) during administration of sulfanilamide: report of two cases. *J. A. M. A.* 109:1009-1011, 1937.
4. Frank, L. J.: Dermatitis from sulfanilamide. *J. A. M. A.* 109:1011, 1937.
5. Schwenker, T. F., and Gelman, S.: Sulfanilamide rash. *Bull. Johns Hopkins Hosp.* 61:136-139, 1937.
6. Mainzer, F. S.: Sulfanilamide rash. *Pennsylvania M. J.* 41:386, 1938.
7. Schlesinger, E. R., and Mitchell, W. L., Jr.: Sulfanilamide eruption study of patients with morbilliform rash and of their subsequent reactions. *Am. J. Dis. Child.* 56:1256-1273, 1938.
8. Tedder, J. W.: Toxic manifestations in skin following sulfanilamide therapy. *Arch. Dermat. & Syph.* 39:217-227, 1939.
9. Garvin, C. F.: Complications following administration of sulfanilamide. *J. A. M. A.* 113:288-291, 1939.
10. Gallagher, J. R.: Sulfanilamide drug fever: second attack of sudden onset. *New Eng. J. Med.* 221:132, 1939.
11. Steven, R. A.: Sensitization to sulfanilamide: report of case. *California & West. Med.* 50:419, 1939.
12. Thompson, A. R.: M & B 693 rashes, with particular reference to acute exanthemata. *Brit. M. J.* 2:13, 1939.
13. Erskine, D.: Dermatitis from sulphonamide compounds. *Brit. M. J.* 2:104-107, 1939.
14. Loveman, A. B., and Simon, F. A.: Fixed eruption and stomatitis due to sulfanilamide. *Arch. Dermat. & Syph.* 40:29-34, 1939.

REPORT ON MEDICAL PROGRESS

REGIONAL ANESTHESIA

ALDEN W. SQUIRES, M.D.*

NEW YORK CITY

SPINAL ANESTHESIA

LAST year the progress report¹ with this title summarized the current status of spinal anesthesia. Subsequent contributions to this subject have made available additional means for producing spinal anesthesia and a better understanding of its physiological effects.

To avoid the difficulties that occur when spinal anesthesia either fails to "take" or wears off too soon, Lemmon² has devised a technic for achieving "continuous spinal anesthesia." The lumbar puncture needle remains in situ during the operation. The anesthetist periodically renews the anesthesia, as need arises, by injecting increments of the anesthetic solution through a tubing attached to the needle. The procedure requires the use of four especially designed articles of equipment: a German-silver needle, malleable enough to adapt itself to changes in the spinal curvature and large enough to exert the friction necessary for keeping it firmly in place when the patient's position is changed; an introducer of the Sise type to facilitate passing the semiflexible needle through the denser tissues of the back; 75 cm. of fine-bore rubber tubing, which is inelastic enough to resist bulging and kinking; an operating table cushion in which a "cut out" section provides space for the needle and tubing when the patient is laid supine for operation.

Lemmon's first report followed his experiences

with 200 cases, in which novocain was used exclusively. It was observed that "the initial injection of novocain has more toxic effects than subsequent injections." Aside from its obvious clinical advantages, this technic promises to offer opportunities for observing the variable effects of comparable doses of anesthetic agents in different persons and emphasizes the factor of individual susceptibility to drug action that is so frequently noted in anesthesia practice.

Lemmon³ has now had experience with 500 cases "without any difficulties in producing anesthesia to the level and extent desired, and every operation was completed under spinal anesthesia." He states:

We are using a 5 per cent solution of novocain crystals dissolved in cerebrospinal fluid. . . . We use this method in all cases that we give spinal anesthesia to. . . . The ability to rapidly withdraw the drug if toxic symptoms develop we believe to be very important. . . . We have observed no cases of motor or sensory disturbances following the use of novocain in this method. . . . We believe this anesthesia permits more satisfactory surgical procedures with lower mortality and morbidity rates.

At the Lahey Clinic the method has been used for sixty-five operations of a variety of kinds.⁴ The following drugs have been employed: Pontocaine (0.25 per cent solution, made hyperbaric with 10 per cent dextrose solution), Metycaine (3 and 5 per cent solutions) and novocain (2.5, 3, 5, 7 and 10 per cent solutions). It was found

*Director of anesthesia, Memorial Hospital, New York City.

that the anesthetic effect of Metycaine apparently lasts a little longer than that of novocain, and that regardless of its concentration about 4 cc. of the anesthetic solution seems to be required to produce full abdominal anesthesia. The total dosage often exceeds that which would be permissible if it were given in a single injection, but no intercostal paralysis, delay in recovery or toxicity has been noted. Larger needles than Lemmon's have been devised and found more satisfactory. The longest operation in the series was a gastric resection, which was prolonged to four and a half hours because two previous gastric operations had made the surgical procedures extremely difficult. The total dosage in this case was 900 mg. of novocain, which was used in a 10 per cent solution. In one case in which 1650 mg. of novocain was used and in another in which there was failure to produce anesthesia, the peculiar results were ascribed to faulty technic in placing the needle.

The introduction of Intracain (Squibb) makes available another agent for regional anesthesia. "Experimental investigations showed Intracain to be slightly more toxic than procain but effective in lower concentrations, longer in action and capable of greater diffusion. Consequently it has a higher anesthetic index."⁵ When administered subcutaneously to mice the minimum lethal dose of Intracain is approximately 70 per cent that of procaine, but the duration of anesthesia produced by nerve block in guinea pigs with a 1 per cent solution of Intracain is reported to be 59 minutes, in contrast to 16 minutes with a 1 per cent solution of procaine hydrochloride.⁶ "Preliminary observations during 100 anesthetics indicate that Intracain may be a useful drug for spinal anesthesia."⁷

Recent studies by Smith et al.⁸ explain the effects of spinal anesthesia on the circulation and suggest the advisability of "the essentially complete abandonment of the view that vasomotor impulses from the central nervous system are necessary, in a subject at rest, to maintain the peripheral arteriolar bed in its normal tonic state . . . provided the method of denervation is not such as to precipitate severe circulatory disturbance." Another important observation is that "the peripheral vasomotor system in man under spinal anesthesia is highly resistant to hypercapnia and anoxemia." More recently Doud and Rovenstine⁹ have reported that spinal anesthesia up to mid-dorsal levels has "little effect upon the velocity of blood flow," but that anesthesia above the sixth thoracic segment may considerably increase circulation time. When this occurs, the administration of ephedrine is effective in restoring normal conditions.

REGIONAL ANESTHESIA IN OBSTETRICS

Spinal anesthesia has not been generally favored for relief of pain in childbirth, although some of the criticisms seem unjustified. The idea that uterine contractions force the drug up the spinal canal into the medulla is not consistent with accepted facts of cerebrospinal-fluid dynamics. Neither could bearing-down efforts have this effect, since exertions of that type are familiarly known to increase intracranial pressure, and since if there is opportunity for its movement, the cerebrospinal fluid then receives an impetus to move caudad.

The major disadvantages of spinal anesthesia in obstetrics are as follows: a possible difficulty in administering it to a restless patient; a relatively brief duration, which makes it inappropriate except for the second stage of labor; a difficulty in ascertaining precisely the proper moment for administration, especially to multiparas whose progress into and through the second stage may be rapid; some retardation of the progress of labor, for although uterine contractions are unimpaired the paralyzed abdominal muscles are unable to perform their important accessory expulsive function.

For such reasons spinal injection, which is an unsuitable method for producing analgesia for an uncomplicated delivery, especially in the home, may, on the other hand, have distinct value when labor is to be terminated operatively. Cosgrove et al.¹⁰ enumerate the advantages that spinal has over inhalation anesthesia under such circumstances: lessened post-partum vomiting, ileus and distress; minimized bleeding; good preservation of uterine tone; maintenance of the patient's conscious co-operative efforts; absence of jeopardy to the baby's condition. Further advantages are evident if the patient presents one of the conditions generally understood to interdict the use of general anesthesia, such as respiratory-tract infection, full stomach, active vomiting and so forth.

The production of regional anesthesia by methods other than spinal injection appears, theoretically at least, to be almost the ideal means of relieving labor pain. In practice such methods have not been employed so widely as they deserve to be, partly because the technics are not generally familiar and partly because none are invariably successful even in the most experienced hands. But there are enthusiasts who proclaim that regional anesthesia in obstetrics is "far superior to inhalation anesthesia."¹¹

Very effective obstetric analgesia should be produced by the technic for pudendal block described by Urnes and Timerman.¹² They found it especially suitable for use in breech delivery,

though contraindicated by threatened rupture of the uterus, severe fetal asphyxia and inflammatory disease of the perineum. Abrams¹³ outlines another technic that produces thorough relaxation of the levators and other perineal muscles, making it unnecessary to "iron out" the perineum. Fewer and smaller episiotomies are required, and there is increased ease in rotating the head with forceps, especially from occiput-posterior positions.

Baptisti¹⁴ reported 200 cases in which analgesia was produced by caudal injection alone. Thirty cubic centimeters of 1 per cent novocain was injected epidurally into the sacral canal. In 182 cases this measure alone provided "satisfactory" anesthesia, although 17 of the cases so classified required supplementary measures. The series included 146 full-term deliveries, in which 123 elective episiotomies, 107 low-forceps applications, 14 mid-forceps applications, 10 breech extractions and 8 low-cervical cesarean sections were done. There was no maternal or infant mortality. The author believes caudal anesthesia to have these advantages: satisfactory pelvic and perineal anesthesia, painless uterine contractions, marked perineal relaxation, maximal uterine tonicity, minimum blood loss and no motor paralysis. One patient had bladder atony for twenty-four hours postpartum.

USE OF REGIONAL ANESTHESIA FOR PURPOSES OTHER THAN IMMEDIATE OPERATIVE PROCEDURES

As in the past, surgeons continue to develop and to find new uses for anesthesia procedures, and to extend their application beyond the relief of actual operative pain. Some of these uses, such as certain complex nerve blocks with alcohol, properly remain in the hands of the skilled neurosurgeons who developed them. But, as recognition of anesthesiology as a medical specialty increases, it is being more generally accepted that the use of anesthetic maneuvers for any purpose is properly the concern and the task of the anesthetist. The anesthetist, however, gratefully acknowledges his debt to surgical practitioners, who from the time of the introduction of ether have been doing most of the pioneer work in his field.

THERAPEUTIC USES

The recent book of Leriche¹⁵ contains the results of his years of study of the phenomena of pain and the effects of trauma. The importance of his theories is being increasingly recognized. According to Leriche not only the subjective sensations of pain but also much of the pathologic anatomy of traumatic lesions is ascribable to abnormal nervous activity. The centripetal flow of pain impulses irritates the sympathetic system

through central reflex pathways and causes vascular spasm at the site of injury. Vasospasm itself aggravates the sensation of pain. Furthermore, as Ochsner and DeBaKey¹⁶ have now clearly substantiated, vasospasm is the chief factor in causing edema at the site of injury. The onset of edema initiates a vicious circle, in which the local circulatory disturbances and the production of pain stimuli accentuate and perpetuate each other.

The clinical importance of this theory is demonstrated by case reports indicating that interruption of the nerve pathways involved in this reflex yields gratifying therapeutic results, since the pain, the local swelling and the functional disability are all simultaneously relieved. This subsidence of the noxious features of traumatic lesions occurs when either the afferent pathways from or the efferent vasomotor pathways to the site of injury are blocked.

Infiltration of local anesthetic agents into the proximity of the lesion is effective and is probably the simplest of these measures. It relieves both the pain and the clinical manifestations of minor fractures, sprains, contusions, and articular and synovial injuries. In a recent review Outland and Hanlon¹⁷ advocate the injection of from 10 to 30 cc. of 1 or 2 per cent solution of procaine hydrochloride at the site of maximum tenderness. Active movement of the injured part is resumed immediately and is usually painless. Subsequent infiltrations are made daily so long as symptoms persist. The fractures suitable for this treatment are those which do not require accurate reduction or immobilization, such as those of lumbar transverse processes, vertebral spinous processes, the head of the radius, epicondyles and malleoli.

In 100 consecutive cases of "minor fractures" reported by Cullumbine¹⁸ treatment consisted of the injection of a 2 per cent solution of novocain between and around the ends of the fragments, and the immediate resumption of full range of active motion. The cases included fractures of the malleoli, bones of the hands and feet, ribs, fibulas and femoral trochanters. No displacement of fragments occurred, and the period of disability was reduced. Cullumbine also reports satisfactory results in the treatment of sprains by infiltration of the injured ligaments with local anesthetic.

Frankel¹⁹ found that all signs and symptoms of severe ankle sprains disappear within a few minutes after injection of a 2 per cent novocain solution into the ligaments. The joint is then firmly strapped, and the patient becomes ambulatory immediately. Outland and Hanlon¹⁷ believe that this procedure has diagnostic value in making it possible to distinguish those cases in which an ac-

tual tear of the ligament has occurred and in which, therefore, immobilization is the treatment of choice.

As with traumatic lesions, the edema, heat, pain, tenderness and loss of function caused by inflammatory lesions subside when sensory impulses from the affected area are interrupted by local anesthetics. Recent reports describe the favorable results obtained with infiltration of anesthetic solutions into the immediate neighborhood of the lesions of bursitis,¹⁷ arthritis¹⁷ (including old stiffened joints and gonococcal lesions²⁰), pleuritis associated with pneumonia or pulmonary infarct,²¹ and furuncles and other local inflammations.²²

Methods that produce regional anesthesia by intercepting somatic pain impulses at points central to the lesion itself should theoretically be as effective as local infiltration, and apparently have been so when properly employed. Because of the greater technical difficulties inherent in such methods, however, they have not been so popular as the simpler infiltrations. Allen and Tuohy²³ have reported several cases in which various types of somatic pain were relieved by brachial-plexus block, paravertebral block or injection of the sciatic nerve. Rovenstine and Byrd²⁴ recommend paravertebral block with procaine and alcohol at the appropriate thoracic levels for the relief of pain and disability with fractured ribs.

Reference has been made to Leriche's contention that reflex sympathetic impulses, by initiating local vasospasm, are an important factor in causing the abnormal circulation and fluid distribution, which in turn produce many of the clinical manifestations of traumatic and inflammatory lesions. It is also contended that these abnormalities of circulation explain the peculiar fact that pain sensations arise in these lesions long after the original stimulus has ceased to operate. The validity of these contentions is apparent in recent reports of the use of regional anesthesia for blocking sympathetic pathways alone.

Campbell²⁵ outlines the technic for and reports his results in blocking the lumbar sympathetic ganglia with procaine as a means of treating severe sprains and first degree fractures of the ankle. Although no cutaneous sensory anesthesia was produced thereby, relief of pain was rapid and at times permanent after one injection, and although deep tenderness persisted, fixation and spasm at the site of injury were completely abolished. The procedure was also effective in relieving the severe pain following arthrodeses and other orthopedic operations on the lower extremities. Campbell believes that, in addition to the factor of reflex vasospasm, some chemical change within the tissues

also occurs at the site of the injury that perpetuates the clinical manifestations and that is abolished when the abnormal sympathetic activity is interrupted.

Ochsner and DeBakey¹⁶ have demonstrated that the clinical features of thrombophlebitis are due chiefly to reflex sympathetic vasoconstrictor impulses initiated by sensory impulses arising in the thrombosed segment. In 17 cases of incapacitating thrombophlebitis "the results obtained by procaine hydrochloride block of the regional sympathetic ganglions were quite dramatic." Following the treatment 6 patients were immediately and permanently relieved of pain. In 11 cases pain cured; 8 of these were permanently relieved after one more treatment and the others by two. In about half the cases, the temperature became normal within forty-eight hours after the first treatment. "Sixty per cent of the patients were discharged from the hospital within eight days after the institution of therapy."

As a means of treating herpes zoster, Rosenak²⁶ injected a 0.5 per cent solution of procaine into the sympathetic chain and ganglia at the appropriate levels in 22 patients. Except in two cases the pain ceased, and the vesicles dried within twenty-four to forty-eight hours. Since this procedure is neither simple nor entirely without danger, it should be used only when there is particularly severe pain.

DIAGNOSTIC USES

Steindler²⁷ contends that "sciatica" is frequently a reflex radiation along the sciatic nerve of impulses that are initiated by disease in adjacent structures. Injury to any one of six sites in the lower back may cause typical sciatic radiation of pain, even when the pathologic process does not involve the sciatic fibers at any point. The actual site of injury is suggested by finding a "trigger point" at which pressure elicits an exaggeration of the sciatic pain, and the location is confirmed when the injection of 3 cc. of a 1 per cent novocain solution into the area is followed by cessation of pain along the sciatic nerve. The author believes this test to be of distinct value, since it enables the surgeon to direct appropriate treatment toward the primary cause of the symptomatology.

Haggart²⁸ has used perineural injection of the sciatic nerve as both a diagnostic and therapeutic measure in dealing with cases of sciatic pain of undetermined cause. He injects approximately 53 cc. of a 1 per cent novocain solution into each of three sites to infiltrate thoroughly the muscle and fascia adjacent to the nerve. The particular value of this procedure is that it provides imme-

diate relief while further diagnostic studies are in progress. When combined with orthopedic manipulation of the spine, it may become adequate therapy for some cases.

Gage²⁹ reports that the injection of novocain into the anterior scalene muscle is an important step in confirming the diagnosis of the scalenus-anticus syndrome that he described in 1935. Elimination of spasm in this muscle relieves the neuro-circulatory disturbance caused by compression of the brachial plexus and the subclavian artery, and thus provides an indication for surgical division of the muscle.

Regional anesthesia procedures that block the sympathetic pathways to the intestinal tract have proved useful in dealing with conditions in which adynamic distention or ileus is conspicuous. When the sympathetic inhibitory components of the autonomic innervation are thus paralyzed, the parasympathetic motor components are given free play to reactivate peristalsis. Distention due to functional obstruction may be relieved in this manner, and the transition of functional ileus into actual obstruction may be prevented. Such treatment provides a period of respite during which the bowel wall, rendered ischemic and atonic as a consequence of distention, is enabled to regain its tone, blood supply and capacity for motor activity.

Novikov,³⁰ of Leningrad, has reported a series of 139 patients who entered the hospital with "acute intestinal obstruction." The immediate treatment in every case was the injection of from 50 to 100 cc. of a 0.25 per cent solution of procaine hydrochloride into the renal fossas to produce a sympathetic block. This treatment alone or in conjunction with the use of enemas made possible the recovery of 76 patients (55 per cent) without surgical intervention. It was valuable also in indicating immediate surgical treatment for the remainder of the group.

Essentially the same results may be obtained by the simpler measure of inducing spinal anesthesia. Because of this fact, there is an increasing tendency to recognize spinal anesthesia as the procedure of choice in dealing with conditions in which distention is an outstanding feature. If there is no known organic lesion to indicate immediate surgery, and if spinal anesthesia or any other method of sympathetic nerve block results in passage of flatus or feces and the relief of the abdominal distention, there is justification for the postponement of surgery and the continuation of conservative treatment. If the obstruction is organic and the distention mechanical, however, spinal anesthesia or another method of sym-

thetic nerve block provides more favorable operating conditions than does ether anesthesia. Nerve block promotes the recovery of peristaltic activity; on the other hand, it was noted many years ago that ether exerts a paralyzing effect on the bowel wall and tends to favor the occurrence of distention.

In chronic adynamic conditions of the bowel, such as Hirschsprung's disease, sympathetic nerve blocks have also been found useful. With their effects noted, it may be possible to predict the outcome of a proposed sympathectomy, or even to make such an operation unnecessary. Climesco, Sarbu and Roman³¹ have recently reported the unusual case of a twelve-year-old child with findings typical of Hirschsprung's megacolon. After the induction of spinal anesthesia the patient's evacuations became normal and remained so for sixteen days. Then a second administration caused a remission for nearly four months.

Spinal anesthesia or some other effective method of producing sympathetic nerve block has been helpful in handling cases of vasospastic disorders of the extremities, particularly of Buerger's disease. The increased skin temperature that follows paralysis of abnormal vasoconstrictor activity provides valuable information as to the extent of improvement that may be anticipated from surgical treatment.

CONCLUSION

Livingston³² in 1934 called attention to the peculiar fact that "in nerve-blocking methods, we have outgrown our name, . . . for what interest have we in *anesthesia* when by carefully directed injections we seek to alter the blood supply to a part?" Since that time it has become even more apparent that nerve-block procedures are highly useful as diagnostic, prognostic and therapeutic procedures, as well as for the alleviation of pain during surgical operations. Livingston aptly summarized the significance of progress in regional anesthesia by stating: "The fundamental basis for [the] importance of regional anesthesia lies in the fact that through nerve injections we may voluntarily bring about the isolation of any region or organ from the remainder of the body. Thus the subject comes to encompass every specialty and separate domain of medicine."

444 East 68th Street

REFERENCES

1. Squires, A. W.: Regional anesthesia. *New Eng. J. Med.* 221:926-931, 1939.
2. Lemmon, W. T.: A method for continuous spinal anesthesia. *Ann. Surg.* 111:141-144, 1940.
3. *Ideo*: personal communication.
4. Nicholson, M. J.: personal communication.

5. Rovenstine, E. A., and Cullen, S. C.: The clinical application of beta-diethylaminoethyl P-ethoxy benzoate hydrochlorid in regional anesthesia. *Anesth. & Analg.* 18:86-89, 1939.
6. McIntyre, A. R., and Sievers, R. F.: Toxicity and anaesthetic potency of some alkoxy benzoates and related compounds. *J. Pharmacol. & Exper. Therap.* 61:107-120, 1937.
7. Sappenfield, R. S., and Rovenstine, E. A.: Intracain: its application to spinal anesthesia. *Anesth. & Analg.* 19:48-52, 1940.
8. Smith, H. W.; Rovenstine, E. A.; Goldring, W.; Chasis, H., and Ranges, H. A.: The effects of spinal anesthesia on the circulation in normal, unoperated man with reference to the autonomy of the arterioles, and especially those of the renal circulation. *J. Clin. Investigation* 18:319-341, 1939.
9. Doud, E. A., and Rovenstine, E. A.: Changes in the velocity of the blood flow during spinal anesthesia. *Anesthesiology* 1:82-88, 1940.
10. Cosgrove, S. A.; Hall, P. O., and Gleeson, W. J.: Spinal anesthesia with particular reference to its use in obstetrics. *Anesth. & Analg.* 16:234-237, 1937.
11. Walker, A. T.: Regional anesthesia in the conduct of labor. *Am. J. Obst. & Gynec.* 32:60-67, 1936.
12. Urnes, M. P., and Timmerman, H. J.: Breech delivery: a comparative study of local and general anesthesia. *J. A. M. A.* 109:1616-1618, 1937.
13. Abrams, S. F.: Block of pudendal nerve in obstetrics. *J. Missouri M. A.* 35:81-83, 1938.
14. Baptisti, A., Jr.: Caudal anesthesia in obstetrics. *Am. J. Obst. & Gynec.* 38:642-650, 1939.
15. Leriche, R.: *The Surgery of Pain*. 512 pp. Baltimore: William Wood & Co., 1939.
16. Ochsner, A., and DeBakey, M.: Thrombophlebitis: the role of vasospasm in the production of the clinical manifestations. *J. A. M. A.* 114:117-124, 1940.
17. Outland, T., and Hanlon, C. R.: The use of procaine hydrochloride as a therapeutic agent. *J. A. M. A.* 114:1330-1333, 1940.
18. Cullumbine, H.: Treatment of fractures by local anesthesia. *Lancet* 2:552, 1939.
19. Frankel, E. L.: Treatment of sprains by injection of procaine. *Lancet* 2:597, 1939.
20. Coronedi, L. B.: Recenti acquisizioni relative all'analgesia articolare nel campo della ortopedia. *Arch. di ortop.* 55:473-504, 1939 (abstract, *J. A. M. A.* 114:2601, 1940).
21. Schnur, S.: Deep injection of novocain for relief of pleural pain. *Ann. Int. Med.* 13:845-848, 1939.
22. Reggiani, M. M.: Sulle infiltrazioni di novocaina nel trattamento dei processi infiammatori acuti circoscritti. *Arch. ital. di chir.* 53:1-55, 1940 (abstract, *J. A. M. A.* 114:2343, 1940).
23. Allen, E. V., and Tuohy, E. B.: Relief of somatic pain by local anesthetic. *Proc. Staff Meet., Mayo Clin.* 15:58-69, 1940.
24. Rovenstine, E. A., and Byrd, M. L.: Use of regional nerve block during treatment for fractured ribs. *Am. J. Surg.* 46:303-308, 1939.
25. Campbell, W. G.: Role of sympathetic nervous system in segmental pain. *Lancet* 2:930-932, 1939.
26. Rosenak, S.: Procaine injection treatment of herpes zoster. *Lancet* 2:1056-1058, 1938.
27. Steindler, A.: The interpretation of sciatic radiation and the syndrome of low-back pain. *J. Bone & Joint Surg.* 22:28-34, 1940.
28. Haggart, G. E.: Sciatic pain of unknown origin: effective method of treatment. *J. Bone & Joint Surg.* 20:851-859, 1938.
29. Gage, M.: Scalenus anticus syndrome: diagnostic and confirmatory test. *Surgery* 5:599-601, 1939.
30. Novikov, G. M.: Novocain block in acute ileus. (In Russian.) *Venzh. khir.* 58:506-512, 1939 (abstract, *J. A. M. A.* 115:87, 1940).
31. Climesco, V.; Sarbu, P., and Roman, S.: Importance de la rachianesthésie dans le diagnostic pathogénique du mégacolon: son éventuelle utilisation thérapeutique. *Presse méd.* 47:1118-1120, 1939 (abstract, *J. A. M. A.* 113:1369, 1939).
32. Livingston, E. M.: Regional anesthesia: its place in medicine. *Am. J. Surg.* 23:210-216, 1934.

Erratum

In Dr. Blumgart's article "Report on Medical Progress: Cardiology," appearing in the November 7 issue of the *Journal*, the following changes should be made:

Page 770, column 2, line 6: change word "hour" to "four."

Page 771, column 2, line 31: change "as much as 55 gr." to "over 80 gr."

**CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITAL**ANTEMORTEM AND POSTMORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor***CASE 26461****PRESENTATION OF CASE**

First Admission. A sixty-seven-year-old American farmer entered the hospital complaining of nocturnal dyspnea of four nights' duration.

The patient stated that he had had a penile chancre at the age of nineteen and that he had been treated with pills and local applications for the next year and a half. He remembered no other cutaneous lesions. He remained symptom free until eight years before entry, when his gait became unsteady and staggering and he stood with the feet wide apart. Furthermore, the toes became numb, and he felt weak and had frequent attacks of syncope that lasted for several minutes. The blood serum gave a positive reaction for syphilis, and his physician began an irregular course of treatment spread over the next three years that consisted of "eight arm injections of 606 and about eight hip injections." The patient then moved to another town, stayed for one and a half years, and received injections every five days. Two and half years before admission he developed attacks of diarrhea, shortness of breath on exertion, nocturia and transient ankle edema, and was at times disoriented. A check-up in the Out Patient Department showed positive blood Hinton and Wassermann tests, but a negative spinal fluid test. He was given treatment by his physician and, in addition, injections of liver extract, because both neurological and blood examinations were suggestive of pernicious anemia and the lumbar-puncture findings were not indicative of syphilis of the central nervous system. The diarrhea and numbness in the toes disappeared, but gait disturbances remained. He carried on without incident until four months before admission, when diarrhea returned and persisted. Each of the four nights before entry the patient was unable to sleep because of attacks of breathlessness that compelled him to walk the floor or sit upright to obtain relief. He had gained about 15 pounds in the previous week.

The patient had had diphtheria at thirty years of age. His mother and father had both lived to about eighty and had died of "shock." Two sisters and one brother had died in infancy.

Physical examination showed a pale and thin

man lying propped up in bed in no apparent distress. The veins of the neck were congested. The chest was barrel shaped. The apex of the heart could be felt in the fifth left interspace, 14 cm. from the midline. A tracheal tug was present. Systolic and diastolic murmurs were heard at the base of the heart, with a soft systolic murmur at the apex. The pulmonary second sound was greater than the aortic. The rate was normal, and the rhythm regular; the blood pressure was 160 systolic, 50 diastolic. The peripheral vessels were palpable and tortuous, and their pulsation exaggerated. A systolic thrill was felt in the neck vessels, and a pistol-shot sound was heard in the femoral arteries. Rales were present at the left lung base, with dullness and absent breath sounds at the right base. The abdomen was soft and protuberant, and shifting dullness could be elicited. The prostate was symmetrically enlarged and firm. There was edema of the ankles. The pupils reacted to light and accommodation. Vibration sense was reduced at the ankles and to a lesser degree at the wrists. The right biceps jerk was absent; all others were present and equal. Pinprick perception was normal, and muscle power good. There was a positive Romberg sign. No other neurological findings were recorded.

The temperature, pulse and respirations were normal.

Examination of the urine showed a ++ test for albumin. Examination of the blood showed a red-cell count of 3,280,000 with a hemoglobin of 85 per cent, and a white cell count of 4200. A blood film showed some poikilocytosis and anisocytosis of the red cells. A reticulocyte count was 0.7 per cent. A stool guaiac test was negative.

X-ray examination of the chest showed cardiac enlargement in the region of the left ventricle. The aorta was elongated, slightly dilated and markedly calcified. The fluoroscopist noted a Corrigan type of pulsation. A soft-tissue mass extended to the right of the esophagus in the region of the sterno-clavicular junction, which slightly displaced the trachea. The mass pulsated and did not move with respiration. The aorta was markedly calcified in this region. The left pleural cavity contained a small amount of fluid, and the costophrenic angle on this side was obscured by plate-like increased markings that appeared to be adhesions. An electrocardiographic recording showed normal rhythm, a ventricular rate of 60, a slightly diphasic T₁ and straight ST₂ and ST₃.

The patient spent an uneventful week in the hospital and was discharged improved.

Second Admission (four months later). After discharge the patient was followed in the Out

Patient Department. He was given iron and digitalis and weekly intramuscular injections of liver extract. He felt fairly well, but was never free from ankle edema and shortness of breath. Gradually the symptoms returned, with marked dyspnea and palpitation, easy fatigability and diarrhea, and with fluid accumulating at the lung bases and in the abdomen. At entry an area of retromammary dullness 8.5 cm. wide was noted. A neurological examination during this admission revealed that motor power, light touch and two-point discrimination were normal. Vibration and position sense were reduced on the left. The reflexes were normal. The impression was gained from these findings that there was some evidence of posterior-column disease. Examination of the blood showed a red-cell count of 3,170,000 with a hemoglobin of 82 per cent, and a white-cell count of 2900. A blood film showed slight anisocytosis and a few microcytes, but no macrocytosis. The color index was 1.2, the volume index 1.3, and a hematocrit reading 38 per cent. The blood pressure was 220 systolic, 30 diastolic. The patient was given digitalis and ammonium chloride, and fluids were restricted to 1500 cc. daily. He again improved and was discharged ten days after admission.

Final Admission (four months later). The patient was treated at home by his physician with 15 units of intramuscular liver at weekly intervals and daily doses of $1\frac{1}{2}$ gr. of digitalis, 3 gm. of ammonium chloride and 10 minims of a saturated solution of potassium chloride twice a day. Shortly before entry he had been given a variety of drugs, including Mercupurin suppositories, potassium iodide and iron. One week before admission, itchy purpuric spots appeared on the feet and gradually extended to involve the entire body, with the exception of the mouth. On examination scarlet, nonblanching macules were present on the skin of both feet; the face and scalp were covered with red papules, some being hemorrhagic and pustular; and the arms and hands showed clusters of hemorrhagic papules and pustular bullae. Subconjunctival hemorrhages were present in both eyes. The findings in the heart were unchanged. The liver was palpable four finger-breadths below the costal margin, and there were marked ascites and edema of the lower legs. The consensus was that the skin lesions were due to medication and consistent with an iodide eruption.

Laboratory investigation showed a red-cell count of 2,800,000 with a hemoglobin of 54 per cent, a white-cell count of 4900 and a platelet count of 86,000. A blood film showed moderate anisocytosis, with microcytes predominating, and a few macrocytes. The color index was 0.94, the volume

index 1.1, and the hematocrit reading 27 per cent. The bleeding time was 4 minutes, the clotting time 8 minutes, and the clot retraction normal. The nonprotein nitrogen of the blood serum was 70 mg. per 100 cc. and the protein 5.2 gm. A phenolsulfonephthalein test showed 10 per cent retention of the dye. There was no free hydrochloric acid in a gastric analysis after the administration of histamine.

Despite discontinuation of iodides and local treatment the skin lesions rapidly progressed, forming numerous pustules and large sloughing areas. The patient quickly failed, and died two weeks after admission.

DIFFERENTIAL DIAGNOSIS

DR. HOWARD B. SPRAGUE: One would think, that to make a diagnosis in this case one would have to have only the facts given in the first two sentences of the history—a man with syphilis poorly treated, developed attacks of nocturnal dyspnea. One would assume that he had syphilitic aortitis.

The patient remained symptom-free until eight years before entry, that is, for about forty years after the original infection, when he began to have neurologic signs and symptoms relating to gait, stance, numbness of the toes, syncope and weakness. It was then discovered that the blood serological tests were positive, and he was treated on that basis. It was not until some time later that the whole picture did not seem to be explained on the basis of central-nervous-system syphilis; the blood seemed to be consistent with a primary anemia, for which he was given liver extract, with some improvement. The presenting symptoms that brought him to the hospital were attacks of nocturnal dyspnea, apparently starting suddenly. The physical findings would go with the original diagnosis of syphilitic aortitis. There was congestion of the veins of the neck, which may be evidence of cardiac failure, the superior mediastinal obstruction that occurs with thoracic tumor, aneurysm, constrictive pericarditis or tricuspid disease. The heart was definitely enlarged. The record states that a tracheal tug was present, a finding that would further fit with a diagnosis of aneurysm. Systolic and diastolic murmurs at the base of the heart, with a soft systolic murmur at the apex, were found. In addition there were pulsating peripheral vessels, a systolic thrill in the neck veins, a pistol-shot sound in the femoral arteries and normal cardiac rhythm. The rest of the examination indicates that there was not sufficient evidence on which to base a diagnosis of central-nervous-system syphilis, but that it fitted well with anemia.

X-ray studies revealed a pulsating soft-tissue mass in this region, which was apparently in the region of the innominate artery. The calcified meniscus in the aortic arch was seen very easily, a finding that suggests some degree of dilatation of the aortic root. This examination showed that there was the collapsing type of pulsation in the aorta, but only a slight degree of dilatation. The left pleural cavity contained a small amount of fluid. Dr. Hugo Roesler remarked to me lately that the left pleural cavity is the first place where fluid usually accumulates with left-heart failure during normal rhythm.* The electrocardiogram apparently does not help very much in establishing the diagnosis.

After discharge the patient was treated for the anemia; he felt fairly well, but did not obtain complete relief. Edema and dyspnea persisted, however, and the blood pressure was 220 systolic, 30 diastolic. Of course, in well-marked aortic regurgitation a high systolic pressure is present. Perhaps there was something about the rigidity of the aorta in this patient that influenced the systolic pressure.

The third admission was apparently brought about by the development of the skin eruption and the fact that the patient began to fail. Far be it from me in a description like this to disagree with the dermatologist. I suppose that this was an iodide rash—one that did not improve probably because the patient was very sick; stopping the medicine brought no relief. The blood picture had presumably been somewhat modified by the therapy. But the volume index was over 1, and the color index became normal, although it had previously been 1.2.

The burden of proof is on anyone who says that a patient does not have a syphilitic aorta when aortic regurgitation is found in the presence of positive blood Hinton and Wassermann tests in a man of this age in cardiac failure who has normal rhythm. The picture is complicated by what appears to be a primary anemia, which could increase the peripheral signs of aortic regurgitation. It does not seem as if we needed to invoke other causes of aortic regurgitation,—hypertension and rheumatism,—and it would surprise me a good deal to have Dr. Castleman say that the patient had calcific aortic stenosis, with all this evidence of peripheral vascular collapse and apparently a

high degree of aortic regurgitation. My diagnoses are as follows: syphilitic aortitis, with aneurysm of the innominate artery, a good deal of atherosclerosis and calcification of the aorta, healing in a sense; primary anemia; necrotizing dermatitis, presumably based on iodide therapy; and probably, terminal uremia.

DR. EDWARD F. BLAND: Was blood taken for culture?

DR. BENJAMIN CASTLEMAN: No.

DR. BLAND: The aortic regurgitation apparently increased under observation, and the anemia did not respond to therapy. The aorta did not look so wide as one would like to see. I thought of the possibility of bacterial endocarditis. One usually forgets that that can occur in syphilitic aortitis.

DR. CASTLEMAN: Dr. Sprague, do you think that in severe heart failure there would be so much evidence of ascites?

DR. SPRAGUE: Do I have to put some cirrhosis in there too?

CLINICAL DIAGNOSES

Cardiovascular syphilis.
Aortitis and aortic regurgitation.
Generalized arteriosclerosis.
Cirrhosis of liver, toxic.
Severe iodide dermatitis.

DR. SPRAGUE'S DIAGNOSES

Syphilitic aortitis, with atherosclerosis and calcification.
Aortic regurgitation.
Aneurysm of the innominate artery.
Terminal uremia.
Primary anemia.
Dermatitis, necrotizing, due to iodide therapy.

ANATOMIC DIAGNOSES

Syphilitic heart disease, with aortic regurgitation and left ventricular hypertrophy.
Mural thrombus, right auricular appendage.
Cardiac infarct, healed, left ventricle.
Syphilitic aortitis.
Aneurysms of innominate and subclavian arteries, syphilitic.
Cirrhosis of liver, toxic.
Perihepatitis and perisplenitis.
Ascites.
Hydrothorax, right.
Arteriosclerosis, generalized, marked.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: This patient had an atrophic and cirrhotic liver, with ascites and peripheral edema. The nodules of regeneration were of vary-

*Dr. Roesler stated that he had made this observation but subsequently noted a confirmation of it in a paper by Bedford (Left ventricular failure *Lancet* 11303, 1939), who in 154 cases of left heart failure found hydrothorax in 38—in the left pleural cavity in 18, in the right in 9, and in both in 11. Bedford refers to Lavibond (*Hydrothorax in Cardiovascular Disease*, Thesis; Cambridge, 1938), who stated that left-heart failure with normal rhythm favored left sided pleural effusion, but with auricular fibrillation right-sided effusion. In hypertensive failure with normal rhythm left sided effusion was twice as common as right-sided, with auricular fibrillation right sided effusion was three times as common as left-sided.

ing sizes, the usual finding in this toxic type, but not in the alcoholic. There was nothing to suggest that syphilis played a role in the cirrhosis. So the edema and ascites may have been due to cirrhosis rather than to congestive heart failure. He did have, of course, a large heart, — 550 gm., — with both hypertrophy and dilatation of the left side. There was evidence of severe syphilitic aortitis of the whole aorta, as well as of the aorta in the region of the valve, at which point there was separation of the cusps at the commissures, allowing free regurgitation. As Dr. Sprague predicted, the patient did have an aneurysm of the innominate artery, and also a small aneurysm of each subclavian artery. Superimposed on the syphilitic aortitis was severe arteriosclerosis with marked calcification and ulceration of some of the plaques. The lungs were normal. The coronary arteries were moderately sclerotic, and there was a small healed infarct in the left ventricle. There was also a mural thrombus in the right auricular appendage.

DR. SPRAGUE: Can you tell us whether or not he had Addison's anemia?

DR. CASTLEMAN: He had extensive hyperplasia of the bone marrow, but certainly not the picture that you see in pernicious anemia. Liver insufficiency could, of course, account for the macrocytic anemia. We examined the cord and found no evidence of syphilis or combined-system disease. In the brain Dr. Kubik found three small lesions, each about 4 mm. in diameter, that were very suggestive of the type of infarction seen in subacute bacterial endocarditis.

CASE 26462

PRESENTATION OF CASE

First Admission. A fifty-two-year-old Hungarian laborer was admitted to the hospital complaining of severe joint pains.

The patient was apparently well until four weeks before admission, when he first noted the onset of aching pains located in the ankles, knees, elbows and the first two fingers of the right hand. The pains were worse at night, and were increased following the use of the joint involved. These pains were accompanied by swelling of the ankles and marked anorexia. Previous to the present illness the diet had been adequate and had included meat two or three times a week. The patient apparently drank "quite a bit" of wine but had not touched whiskey for more than nine months prior to admission. He stated that he had always had a "chronic cold," but he com-

plained of no other symptoms. No dyspnea, orthopnea, paresthesia, numbness or tingling or shooting pains were noted.

The patient had pneumonia in 1901 and 1908. The past history showed no other relevant illnesses. The family and marital histories were non-contributory.

Physical examination revealed a well-developed but poorly nourished man in no apparent acute discomfort. The pupils reacted well to light and distance. The mouth contained a few carious teeth. The lungs were clear. Examination of the heart was negative except for a systolic apical murmur. The blood pressure was 120 systolic, 70 diastolic. Examination of the abdomen was negative. The elbows, shoulders, knees and ankles showed limitation of motion and were painful. The fingers showed a suggestion of clubbing, and the ankle and knee joints were swollen and warm. The remainder of the physical examination was negative.

The temperature was 97.6°F., the pulse 82, and the respirations 22.

Examination of the urine was negative. The blood revealed a red-cell count of 5,300,000 with 85 per cent hemoglobin, and a white-cell count of 10,000 with 68 per cent polymorphonuclears. The stools were guaiac negative. A blood Hinton test was negative. The sedimentation rate was 1.5 mm. per minute. An electrocardiogram was normal. The basal metabolic rate was + 2 per cent. The uric acid of the blood serum was 2.8 mg. per 100 cc., the nonprotein nitrogen 24 mg. and the serum protein 6.7 gm.

X-ray examination of the chest revealed hilus shadows that were at the upper limits of normal of width and density. No lymph nodes were visible. The heart was at the upper limits of normal in size. There was a rounded mass — about 5 cm. in diameter — behind the heart near the diaphragm. There were also small rounded shadows scattered over both lungs, more on the right. X-ray study of the bones of the feet showed a hallux-valgus deformity. There was periosteal thickening of the first and fifth toes on both sides, most marked along the shaft of the bone. Similar changes were seen along the proximal phalanges of the second, third, fourth and fifth metatarsals on both sides. The joint surfaces were smooth, and there was no narrowing. There was no definite spur formation. There appeared to be diffuse soft-tissue thickening about the foot and ankle. There were similar periosteal changes at the lower ends of the shafts of the fibula, tibia, radius and ulna on both sides. None of the bones of the hands showed definite abnormality or joint

disease. There was questionable clubbing of the fingers

The patient ran a steadily downhill course during his hospital stay. The bronchoscopic removal of a specimen of the apparent tumor mass of the chest was attempted without success. Following this the patient was given radiation therapy, totaling 600 r to the front and back of the left chest, in an effort to rule out the possibility of the tumor's being a radio sensitive mass. Re-examination of the chest eighteen days after the first chest plate showed that the area of increased density had extended laterally beyond the lateral border of the heart so that it was visible in the anteroposterior view. The lateral view showed no appreciable change. There was marked mottling in the diseased area. The small round areas in the remaining parts of the lung had increased in size. Re-examination of the hands and feet roentgenologically one month after admission revealed that periosteal newbone formation about the distal ends of the radius and ulna on both sides had markedly increased since the previous examination, and that there were similar changes about the metacarpal phalanges. Some of the newly formed periosteal bone had become part of the cortex. The patient was treated with hot packs, bed rest, adequate sedation and analgesics, and was discharged unimproved on the forty seventh hospital day. He ran a picket-fence type of temperature during the latter half of his stay in the hospital. The temperature, which swung daily between 100 and 104°F, gradually fell by lysis and on discharge was 100; the pulse was 90, and the respirations 20.

Final Admission (two months later) The patient re-entered for terminal hospital care. Since discharge he had complained of a gradual but continuous increase in pain in the various joints previously noted. He became incapacitated and had to be lifted onto the bed pan and so forth. The cough increased, and at times blood tinged sputum was seen. He had experienced fever and chilly sensations and, at times, frank chills while at home.

Physical examination revealed a feverish, emaciated, poorly nourished man lying helplessly in bed, who presented huge swellings of the hands and feet, with enlargement of the knees, elbows and shoulder joints. He was slightly pale, the breath was foul, and the teeth were dirty and carious. Palpation revealed a few soft, but large lymph nodes at the root of the neck and one in the right axilla. Examination of the chest showed a few coarse rales anteriorly. The hands and feet were markedly swollen, with moderately pitting

edema. The skin over these joints was shiny. The hands and feet were tender, and there was a marked clubbing of the terminal fingers. The edema extended a little above the wrists and ankles.

Examination of the urine was negative. The blood showed a red cell count of 3,800,000, and a white cell count of 10,200 with 68 per cent polymorphonuclears.

The patient ran a steady and progressive downhill course, and expired on the forty-third hospital day. He was given snake venom intramuscularly and morphine to control pain. The enlarged, swollen, tender joints gradually and continually became smaller and more normal before his exitus.

DIFFERENTIAL DIAGNOSIS

DR. F. DENNETTE ADAMS: At first glance, on the basis of the history, physical examination and laboratory findings, this case seems to be one of rheumatoid arthritis. Rheumatic fever rarely appears for the first time at fifty-two, however. The onset and course are too acute for degenerative joint disease (hypertrophic arthritis), such multiple joint involvement is excessively rare in the initial attack of gout. Polyarthritis is the rule at the onset of gonococcal joint infection, but within a few days most of the affected joints clear completely, the few that remain affected are usually the large joints. The possibility of joint symptoms secondary to some current or recent infection, such as tonsillitis or prostatitis, should be considered. In concentrating on the commoner varieties of joint disturbance we are inclined to overlook acute pulmonary osteoarthropathy, yet it is by no means unusual.

One should be especially suspicious, of course, in any case with a history of chronic bronchopulmonary infection or a symptom like persistent cough (dry or productive) or hemoptysis. In this case we have, to be sure, a story of "chronic cold," but the term is not sufficiently specific to be of any significance.

Physical examination provides no important leads. Definite clubbing of the fingers draws attention to the possibility of pulmonary osteoarthropathy, but the statement that the fingers showed a suggestion of clubbing is hardly specific enough to be taken seriously. If it could be shown that the joint tenderness was actually over the shafts of the bones near the joints rather than over the joints themselves, one would look for pulmonary osteoarthropathy as opposed to arthritis, but only a very careful examination would bring out this distinction.

The systolic apical murmur in a man of fifty-

two can be discounted in the absence of other signs of cardiac disease. The electrocardiogram was probably taken to exclude prolonged auriculo-ventricular conduction time—a finding which is present in about 25 per cent of the cases of acute rheumatic infection.

The roentgenogram quite obviously establishes a diagnosis. Dr. Aubrey O. Hampton informs me that periosteal thickening of the kind described here is typical of pulmonary osteoarthropathy. Similar periosteal thickening occurs in long-standing edema associated with varicose veins, but this would affect only the bones of the legs. The periosteal thickening in syphilis involves only the shafts of the larger long bones. In rheumatoid arthritis, periostitis occurs about the ends of the bones, but is a localized process and occurs only in the presence of obvious changes in the adjacent joints.

DR. TRACY B. MALLORY: It might be fair to say that the x-ray picture is pathognomonic of osteoarthropathy, and to say also that it was diagnosed unhesitatingly by the x-ray department.

DR. ADAMS: It seems perfectly apparent, then, that this case is one of lung tumor with secondary pulmonary osteoarthropathy. Nothing in the clinical picture or roentgenograms points toward any inflammatory process. If my reasoning is correct, —and I fail to see how it could be otherwise,—the real problem is to decide on the nature of the tumor. Is it primary bronchiogenic carcinoma, or is it metastatic tumor from a primary lesion elsewhere? Multiple lesions point toward metastatic disease. Carcinoma of the kidney (hypernephroma) or perhaps of the prostate would be likely sources for the primary tumor. We have no record of a prostatic examination, intravenous pyelogram, gastrointestinal roentgenogram or other procedures in a search for a primary lesion.

Lymphoblastoma is always a possibility. The prolonged fever in this patient is suggestive, but the roentgenograms of the chest are not what one ordinarily sees in lymphoblastoma. The pulmonary lesions of lymphoblastoma are rarely so well circumscribed as the one in this case, and on the rare occasions when circumscribed lesions are found, shadows indicating mediastinal lymph-node involvement should be present. Failure to obtain a favorable response to x-ray therapy also leads one away from a diagnosis of lymphoblastoma, and I think these two important factors together are sufficient to exclude it.

The fever might perhaps be explained on the basis of infection distal to an obstructing lesion in the bronchus, but under such circumstances one would expect more cough and more sputum,

or perhaps roentgenologic evidence of abscess formation.

At the second admission, two months later, the patient was obviously dying of cancer. The cough, bloody sputum, chills and fever indicate progress of the bronchopulmonary disease, and the increasing joint symptoms, further progress of the osteoarthropathy.

The crux of the situation, then, is whether we are dealing with a primary bronchiogenic carcinoma or a metastatic carcinoma; we have very little evidence either way. In the absence of a demonstrable primary lesion elsewhere, despite the fact that the lesions in the lung are multiple, I am inclined to make a diagnosis of primary bronchiogenic carcinoma.

DR. MALLORY: The multiple foci of tumor in this lung do not disturb you?

DR. ADAMS: Yes, they do. That is why I hesitate to make a diagnosis of primary bronchiogenic carcinoma. The extent of the fever also disturbs me, for in my experience, in the absence of severe infection with obstruction, fever is more suggestive of lymphoblastoma. However, when everything is considered, I believe the safest diagnosis is primary bronchiogenic carcinoma.

CLINICAL DIAGNOSIS

Carcinoma of the lung, with hypertrophic pulmonary osteoarthropathy.

DR. ADAMS'S DIAGNOSES

Carcinoma of the lung, probably bronchiogenic.
Pulmonary osteoarthropathy.

ANATOMICAL DIAGNOSES

Carcinoma, probably adenocarcinoma of lung, with intrapulmonary metastases.
Pulmonary osteoarthropathy, severe, generalized.
Bronchopneumonia, acute and organizing.
Emaciation.
Hydrothorax, right.
Pleuritis, chronic fibrous, right.
Arteriosclerosis, slight, generalized.

PATHOLOGICAL DISCUSSION

DR. MALLORY: The post-mortem examination showed a large tumor near the apex of the left lower lobe that had all the gross characteristics of a primary bronchiogenic carcinoma. On microscopic examination we were inclined to interpret it as a very undifferentiated adenocarcinoma. There were multiple foci of metastasis throughout the lungs, but there were no metastases elsewhere in the body. That is a little unusual for a primary bronchiogenic carcinoma, but it is occasionally seen.

If the tumor should reach a hilar lymph node and penetrate into a bronchial or pulmonary artery, metastases might be spread throughout the entire lung.

The bones showed the most extensive periosteal changes that we have seen in this hospital. Around the cortex of the fibula there was a layer of newly formed bone at least 3 mm. thick, almost surrounding the shaft. We are gradually learning that this is a very characteristic phenomenon of pulmonary osteoarthropathy. We have not yet started systematic x-ray studies of patients suspected of having bronchiogenic carcinoma to see if they always have periosteal changes in the fibulas and tibias. I have an idea that if we did we should pick up a lot more than we have in the past.

DR. ADAMS: My impression is that with pulmonary osteoarthropathy one usually finds some degree of infection in the lungs and bronchi. If one sees it in tuberculosis, there is cavitation; in chronic bronchopulmonary disease, there is always bron-

chiectasis or abscess. Does one find pulmonary osteoarthropathy with tumor of the lung in the absence of secondary infection?

DR. MALLORY: I have been more impressed with bronchial obstruction than with infection in such patients. Primary tumors of the lung always start in a bronchus. It is fair to assume that there will be some bronchial obstruction with almost every primary cancer of the lung. Certainly one sometimes sees very acute pulmonary osteoarthropathy quite early in cancer of the lung without any evidence of infection. Metastatic tumors in the lung, on the other hand, rarely occlude bronchi, and pulmonary osteoarthropathy is correspondingly unusual.

One of the junior men in the X-ray Department handled this case extremely well. On seeing the x-rays of the extremities, he immediately re-examined the chest and picked up signs of tumor, which up to that moment no one had thought of as a possibility.

two can be discounted in the absence of other signs of cardiac disease. The electrocardiogram was probably taken to exclude prolonged auriculo-ventricular conduction time—a finding which is present in about 25 per cent of the cases of acute rheumatic infection.

The roentgenogram quite obviously establishes a diagnosis. Dr. Aubrey O. Hampton informs me that periosteal thickening of the kind described here is typical of pulmonary osteoarthropathy. Similar periosteal thickening occurs in long-standing edema associated with varicose veins, but this would affect only the bones of the legs. The periosteal thickening in syphilis involves only the shafts of the larger long bones. In rheumatoid arthritis, periostitis occurs about the ends of the bones, but is a localized process and occurs only in the presence of obvious changes in the adjacent joints.

DR. TRACY B. MALLORY: It might be fair to say that the x-ray picture is pathognomonic of osteoarthropathy, and to say also that it was diagnosed unhesitatingly by the x-ray department.

DR. ADAMS: It seems perfectly apparent, then, that this case is one of lung tumor with secondary pulmonary osteoarthropathy. Nothing in the clinical picture or roentgenograms points toward any inflammatory process. If my reasoning is correct,—and I fail to see how it could be otherwise,—the real problem is to decide on the nature of the tumor. Is it primary bronchiogenic carcinoma, or is it metastatic tumor from a primary lesion elsewhere? Multiple lesions point toward metastatic disease. Carcinoma of the kidney (hypernephroma) or perhaps of the prostate would be likely sources for the primary tumor. We have no record of a prostatic examination, intravenous pyelogram, gastrointestinal roentgenogram or other procedures in a search for a primary lesion.

Lymphoblastoma is always a possibility. The prolonged fever in this patient is suggestive, but the roentgenograms of the chest are not what one ordinarily sees in lymphoblastoma. The pulmonary lesions of lymphoblastoma are rarely so well circumscribed as the one in this case, and on the rare occasions when circumscribed lesions are found, shadows indicating mediastinal lymph-node involvement should be present. Failure to obtain a favorable response to x-ray therapy also leads one away from a diagnosis of lymphoblastoma, and I think these two important factors together are sufficient to exclude it.

The fever might perhaps be explained on the basis of infection distal to an obstructing lesion in the bronchus, but under such circumstances one would expect more cough and more sputum,

or perhaps roentgenologic evidence of abscess formation.

At the second admission, two months later, the patient was obviously dying of cancer. The cough, bloody sputum, chills and fever indicate progress of the bronchopulmonary disease, and the increasing joint symptoms, further progress of the osteoarthropathy.

The crux of the situation, then, is whether we are dealing with a primary bronchiogenic carcinoma or a metastatic carcinoma; we have very little evidence either way. In the absence of a demonstrable primary lesion elsewhere, despite the fact that the lesions in the lung are multiple, I am inclined to make a diagnosis of primary bronchiogenic carcinoma.

DR. MALLORY: The multiple foci of tumor in this lung do not disturb you?

DR. ADAMS: Yes, they do. That is why I hesitate to make a diagnosis of primary bronchiogenic carcinoma. The extent of the fever also disturbs me, for in my experience, in the absence of severe infection with obstruction, fever is more suggestive of lymphoblastoma. However, when everything is considered, I believe the safest diagnosis is primary bronchiogenic carcinoma.

CLINICAL DIAGNOSIS

Carcinoma of the lung, with hypertrophic pulmonary osteoarthropathy.

DR. ADAMS'S DIAGNOSES

Carcinoma of the lung, probably bronchiogenic.
Pulmonary osteoarthropathy.

ANATOMICAL DIAGNOSES

Carcinoma, probably adenocarcinoma of lung, with intrapulmonary metastases.
Pulmonary osteoarthropathy, severe, generalized.
Bronchopneumonia, acute and organizing.
Emaciation.
Hydrothorax, right.
Pleuritis, chronic fibrous, right.
Arteriosclerosis, slight, generalized.

PATHOLOGICAL DISCUSSION

DR. MALLORY: The post-mortem examination showed a large tumor near the apex of the left lower lobe that had all the gross characteristics of a primary bronchiogenic carcinoma. On microscopic examination we were inclined to interpret it as a very undifferentiated adenocarcinoma. There were multiple foci of metastasis throughout the lungs, but there were no metastases elsewhere in the body. That is a little unusual for a primary bronchiogenic carcinoma, but it is occasionally seen.

The epidemic, tuberculosis, is young when it makes its first encounter with a population, it matures when its contact has become fairly universal for a few generations, and it is old when the population as a whole has become so resistant to its ravages that the death rate falls rapidly. Earliest childhood, maturity and senescence of tuberculosis are represented by the early invasion by tuberculosis of certain African tribes and a group of American Indians, the American Negro and our own white population.

Wherever tuberculosis strikes first, it is in primitive societies. By "primitive" is meant a society previously not or hardly in contact with the occidental civilization and a society that for a long period has lived in essentially unchanged, settled conditions—a population without history in the common sense of the word. Tuberculosis never comes alone to an untouched population; it always is accompanied by, and rather through agents of occidental civilization. It is, therefore, always associated with profound changes and disturbances of tribal life. These changes play a most significant role in shaping the epidemic features.

Borrel reports that a portion of Senegalese troops were tested with tuberculin on arrival in France during the last war, and only 4 to 5 per cent reacted. Many of these men were observed at a later date as tuberculous patients and on the autopsy table. The general picture was about as follows. Following a certain period without evident clinical symptoms, during which swellings of supraclavicular and tracheobronchial lymph nodes can be observed, the disease develops rapidly with toxemia, high fever, weakness and multiple organ involvement that in 70 per cent lead to death. At autopsy diffuse caseation of multiple groups of lymph nodes is dominant in 70 to 90 per cent of the cases. One fourth of the patients died of generalized miliary tuberculosis, and in a large proportion of the remainder diffuse caseous foci were present. Here is a form of disease characterized clinically by the predominance of systemic over local symptoms by the rapidity of its course and by its high fatality. The characteristics are generalization, diffuse caseation and the absence of reparative processes.

However, the majority of Senegalese neither acquired nor died of tuberculous disease, and it is safe to assume that many healthy reactors returned to Africa proving their resistance to tuberculous infection.

A somewhat later stage than that of practically universal infection, is represented by an epidemic among certain Indian tribes of the Canadian plains. Following a period (1850–1880) in which there were only sporadic cases of tuberculosis, the epidemic reached its height between 1884 and 1890, during which time one out of three Indians had visible lymph node swelling, and by 1906 about 20 per cent of the school children in Qu'Appelle were operated on for tuberculous nodes. The death rate rose from 1000 in 1881 to 9000 in 1886 falling to 2000 in 1901 and to 1000 in 1907, following the establishment of antituberculous work in 1930, it reached 270 in 1931–32.

The most complete epidemiological studies of tuberculosis in a relatively primitive society were made on the South African tribes that provide the laborers for the mining industry in South Africa. These studies are reviewed by the author. He points out that the epidemiological picture of South African natives is not a uniform one, since these natives have been observed under three different living conditions, namely, in their native villages during labor service in mines and during war service in France. Hence, observations limited to only one of the three localities would lead to an incomplete and biased impression.

A more mature stage of the epidemic is illustrated by tuberculosis as it occurs in the American Negro. The tuberculin index is higher than in the white American, the death rate about three times as high and the peak of the age incidence is earlier. Furthermore, the shift of this peak toward older age groups, although pronounced in the White is negligible in the Negro.

Many Negroes show the same chronic localizing type of disease as the Whites, but relatively acute forms, generalizations in the form of lymphatic and hematogenous spread, occur with much greater frequency in Negroes than in Whites. This was demonstrated by the author in a previous study and in order to confirm these findings, he calculated the ratio of deaths from all forms of tuberculosis to deaths from disseminated tuberculosis separately for the two races. The figures derived from the United States mortality statistics show that the relative frequency of disseminated forms is considerably higher in Negroes and that the decrease of disseminated forms during the last seventeen years is much smaller in Negroes than in Whites.

Several studies of tuberculosis among Negroes and Whites under identical or similar living conditions show that although the morbidity rates are closely similar, the mortality rate for the Negro is about four times higher than that for the White. One writer concluded that the chances for colored children (in Baltimore) to become infected in a tuberculous family are about equal to those of white children under similar circumstances, but the chances of dying from tuberculosis are three times greater in colored than in white children.

Lack of space prohibits quotation of the author's discussion based on his observations, but the following points stand out.

In the early phases of tuberculosis the disease is acute rapidly fatal, generalized without tendency to heal with toxic symptoms overshadowing local symptoms and has a predilection for the young.

No nation or tribe free of tuberculosis has a uniformly high susceptibility to tuberculosis. The complete lack of resistance in so-called "virgin soil" is a myth. The individual degree of resistance and the collective frequency of the disease are not simply matters of interplay between host and bacillus but they are profoundly influenced by living conditions in the widest sense of the word.

The most spectacular decrease in tuberculosis mortality occurred as a rule, before any organized campaign against tuberculosis could be initiated. However, anti-tuberculosis work is undoubtedly effective in later phases of the epidemic.

The South African report makes it clear that previous infection did in no noticeable way, modify or alter tuberculous disease that developed later. A primary infection in a not highly resistant stock produces allergy without causing immunity.

There is no shred of evidence to show that immunization is transmitted by heredity. The elimination of the least resistant strains must undoubtedly play an important role in the gradual attenuation of tuberculosis, particularly in the early phases of the epidemic.

Tuberculosis mortality parallels the socio-economic conditions so much so that it would seem that poverty and unusual stress and strain should be the guideposts for case finding programs.

There is little danger that an acute and virulent epidemic may sweep again through our population some time after tuberculosis has been eliminated (or reduced to its minimum) because the immunizing effects of infection would

then be lost. A population that has survived a tuberculosis epidemic and has rid itself of it is hardly comparable to a "virgin-soil" population.—Reprinted from *Tuberculosis Abstracts*, November, 1940.

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR SEPTEMBER, 1940

DISEASES	SEPTEMBER 1940	SEPTEMBER 1939	FIVE-YEAR AVERAGE*
Anterior poliomyelitis	15	20	141
Chicken pox	105	84	81
Diphtheria . . .	7	15	15
Dog bite	977	923	863
Dysentery, bacillary	17	56	20
German measles	18	21	28
Gonorrhea	391	419	516
Lobar pneumonia	135	82	113
Measles	211	73	82
Meningococcus meningitis	4	2	4
Mumps	125	62	141
Paratyphoid B fever	3	5	10
Scarlet fever	127	98	162
Syphilis	403	335	441
Tuberculosis, pulmonary	270	215	237
Tuberculosis, other forms	32	24	25
Typhoid fever	5	9	14
Undulant fever	9	1	2
Whooping cough	474	403	427

*Based on figures for preceding five years.

RARE DISEASES

Actinomycosis was reported from: Lawrence, 1; total, 1.

Anterior poliomyelitis was reported from: East Longmeadow, 1; Fall River, 1; Norfolk, 1; North Adams, 1; Springfield, 2; Westhampton, 1; Worcester, 8; total, 15.

Anthrax was reported from: Lowell, 1; total, 1.

Diphtheria was reported from: Auburn, 1; Beverly, 1; Malden, 1; Pittsfield, 2; Somerville, 1; Taunton, 1; total, 7.

Dysentery, bacillary, was reported from: Boston, 2; Chelsea, 1; Lawrence, 1; Lowell, 4; Medford, 7; Randolph, 1; Wrentham, 1; total, 17.

Infectious encephalitis was reported from: Medford, 1; Springfield, 1; total, 2.

Malaria was reported from: Boston, 1; total, 1.

Meningococcus meningitis was reported from: Brockton, 1; Cambridge, 1; Fitchburg, 1; Harwich, 1; total, 4.

Paratyphoid B fever was reported from: Boston, 2; Dartmouth, 1; total, 3.

Pellagra was reported from: Boston, 1; total, 1.

Septic sore throat was reported from: Boston, 2; Cambridge, 1; Wrentham, 1; total, 4.

Tetanus was reported from: Bourne, 1; Revere, 1; Somerville, 1; total, 3.

Trichinosis was reported from: Boston, 1; Fall River, 1; total, 2.

Typhoid fever was reported from: Malden, 1; Quincy, 1; Somerville, 1; Weymouth, 1; Woburn, 1; total, 5.

Undulant fever was reported from: Chelsea, 1; Natick, 1; North Adams, 1; Northbridge, 1; Provincetown, 1; Sherborn, 1; Shrewsbury, 1; Southbridge, 1; Taunton, 1; total, 9.

Anterior poliomyelitis continued to show low incidence. Lobar pneumonia, pulmonary tuberculosis, tuberculosis (other forms), measles and chicken pox were reported above the five-year averages.

Diphtheria was reported at a record low figure, except for that of 1937, which was equaled.

German measles, scarlet fever, mumps, bacillary dysentery and paratyphoid B fever were reported below the five-year averages.

Typhoid fever showed record low incidence.

Undulant fever was reported at a record high figure.

Dog bite was reported at a record high figure for the second consecutive month. Animal rabies showed low incidence. Active foci were noted in Hingham and East Bridgewater.

NOTES

Dr. G. Lynde Gately, of East Boston, has been appointed health commissioner of the City of Boston; he succeeds Dr. Henry F. R. Watts, who has retired on a pension after having served the city thirty-one years in one or another capacity pertaining to the health of its inhabitants.

The American Public Health Association has recently announced the posthumous award of the Sedgwick Memorial Medal to Dr. Hans Zinsser.

CORRESPONDENCE

SULFANILAMIDE SPRAY

To the Editor: Sulfanilamide, applied locally, has been used with success in the treatment of infected wounds. I occurred to me that the local application of the drug might be of benefit in colds and sore throats. For the past month I have been using a spray containing 15 gr. of sulfanilamide dissolved in an ounce or an ounce and a half of warm water. It does not dissolve completely and is liable to clog the atomizer at times, but this can be remedied by blowing through the stem.

Of all the sprays I have ever used this seems to be by far the most efficient. Head colds, if treated early, clear up rapidly with no other treatment. I can testify that it is the only local application that I have found to be effective in the treatment of a stubborn pharyngitis.

NEIL C. STEVENS.

Walpole, New Hampshire.

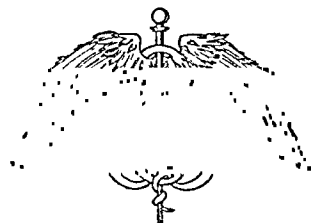
NOTICES

THE BOSTON DISPENSARY

There will be a clinical staff meeting of the Boston Dispensary in the Pratt Hospital Auditorium on Friday, November 22, at 12:30 p.m. Dr. Leopold Lichtwitz, physician-in-chief, Montefiore Hospital, New York City, will speak on "Certain Aspects of Nephritis." Drs. Henry A. Christian, H. E. MacMahon and Robert W. Buck will discuss the subject. Luncheon will be served at 12.00 m.

Interested members of the profession are invited to attend.

BOSTON DOCTORS' SYMPHONY ORCHESTRA



The Boston Doctors' Symphony Orchestra will rehearse under Alexander Thiede, formerly concertmaster of the Cleveland Symphony Orchestra, every Thursday at 8:30 p.m. Those interested in becoming members should com-

municate with Dr. Julius Loman, Pelham Hall Hotel, Brookline (BEA 2430).

SOUTH END MEDICAL CLUB

The next meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on Tuesday, November 19, at 12 00 m. Dr Walter Bauer will speak on 'Gonorrheal Arthritis Its diagnosis and treatment'. Physicians are cordially invited to attend.

FREE EVENING SPEECH CORRECTION LESSONS

The Institute for Speech Correction Incorporated with the co-operation of Professor Samuel D Robbins's advanced students in speech pathology at Emerson College offers free lessons to any person who is handicapped with any sort of speech defect and is unable to pay the tuition at the institute, upon recommendation of his family physician. Those who can pay a nominal fee will be expected to pay what they can. All applicants will be required to fill out the regular scholarship application form. Classes will meet at 419 Boylston Street, Boston, on Monday evenings the first at 6 00 p m, and others at different hours through the evening.

SALEM TUMOR CLINIC

A teaching clinic on cancer of the head and neck under the sponsorship of the Salem Tumor Clinic will be held at the Salem Hospital on Friday, November 22, at 9 00 a m. The clinic will be conducted by Dr Thomas Anglem.

Members of the Massachusetts Medical Society are cordially invited to attend.

NEW ENGLAND SOCIETY OF PHYSICAL MEDICINE

The regular meeting of the New England Society of Physical Medicine will be held at the Hotel Kenmore, Boston, on Wednesday, November 20, at 8 00 p m. Dinner will be served in the Empire Room at 6 30 p m.

Dr Otto J Hermann will speak on 'Convalescent Care of Fractures, with Special Reference to Physical Therapy'. It will be discussed by Drs Howard Moore and William D McFee.

All members of the medical profession are cordially invited to attend.

NEW ENGLAND PATHOLOGICAL SOCIETY

The next meeting of the New England Pathological Society will be held at the Peter Bent Brigham Hospital on Thursday, November 21, at 8 00 p m. Dr Harry S N Greene, member of the Department of Animal and Plant Pathology of the Rockefeller Institute for Medical Research at Princeton, New Jersey, will speak on 'The Development of Autonomy in Spontaneous Rabbit Tumors'.

ESSAY SOUTH DISTRICT MEDICAL SOCIETY

The dates, subjects, speakers and places for the 1940-1941 medical meetings of the Essex South District Medical Society are listed below. Clinics are held at 5 00 p m, with dinner at 7 00 p m, followed by the speaker of the evening.

December 4 The Diagnosis and Treatment of the Common Arthritides. Dr Walter Bauer. Salem Hospital, Salem.

January 8 Visceral Pain and Its Relief. Dr James C. White. Drivers State Hospital, Hathorne.

February 5 Subject to be announced. Lynn Hospital.

March 5 X-ray in Heart Disease. Dr Merrill C. Sosman. Essex Sanatorium, Middleton.

April 2 Pediatric Problems in General Practice. Dr Joseph Garland. Addison Gilbert Hospital, Gloucester.

May 14 Relation of the Doctor to the Law. Mr Le Ind Powers. New Ocean House, Swampscott.

ROBERT DAWSON EVANS MEMORIAL LECTURE

A Robert Dawson Evans Memorial Lecture will be given by Dr Thomas M Rivers, director of the Hospital of the Rockefeller Institute for Medical Research, New York City, in the Evans Memorial Auditorium, 78 East Concord Street, Boston, on Tuesday, November 19, at 8 15 p m. The subject will be 'Elementary Bodies of Vaccine'.

AMERICAN ACADEMY OF DERMATOLOGY AND SYPHILOLOGY

The third annual meeting of the American Academy of Dermatology and Syphilology will be held at the Palmer House, Chicago on December 8, 9, 10 and 11. There will be over sixty lectures on the program from Monday, December 8, through Wednesday, December 11. Sessions will be in the form of symposiums (special lectures in courses of one to four hours each), numerous luncheon round table discussions and clinical presentations at the University of Illinois Medical School.

Actual cases of rare dermatoses and of other important skin diseases will be presented at the University of Illinois Medical School Monday afternoon, December 9, by a score of leading dermatologists from various parts of the country. These clinical presentations will be arranged so that visiting dermatologists and syphilologists can attend several different presentations during the afternoon. Discussion of rare dermatoses will follow the meeting and will be resumed in the Palmer House that evening.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING SUNDAY, NOVEMBER 17

MONDAY NOVEMBER 18

- 11 30 a m Monthly clinical meeting and luncheon. Carney Hospital.
- 12 15-1 15 p m C of a copathological conference. Peter Bent Brigham Hospital amph theater.
- 8 p m The Orr Treatment of Compound Fractures. Dr Erle Teal. Boston Orthopedic Club. Boston Medical Library & Fenway.

TUESDAY NOVEMBER 19

- 9-10 a m The Present Status of Urinary Tract Calculi. Dr H W Sulkowitch. Joseph H Pratt Diagnostic Hospital.
- 12 m Gonorrheal Arthritis Its diagnosis and treatment. Dr Walter Bauer. South End Medical Club. Headquarters of the Boston Tuberculosis Association. 554 Columbus Avenue. Boston.
- 12 15-1 15 p m Clinical genitological conference. Peter Bent Brigham Hospital amph theater.
- 8 15 p m Elementary Bodies of Vaccine. Dr Thomas M Rivers. Robert Dawson Evans Memorial Lecture. Evans Memorial Auditorium. 78 East Concord Street. Boston.

WEDNESDAY NOVEMBER 20

- 9-10 a m Hospital case presentation. Dr S J Thannhauser. Joseph H Pratt Diagnostic Hospital.
- 12 m Clinical pathological conference. Children's Hospital.
- 4-4 p m Anemia. Drs W P Murphy and Robert Zellinger. Peter Bent Brigham Hospital.
- 8 p m Boston Society of Biologists. Biological Laboratories. Divinity Avenue. Cambridge.
- 8 p m Convalescent Care of Fractures with Special Reference to Physical Therapy. Dr Otto J Hermann. New England Society of Physical Medicine. Hotel Kenmore. Boston.

THURSDAY NOVEMBER 21

- 8 30 a m Combined clinic of the medical, surgical and orthopedic services of the Children's Hospital and the Peter Bent Brigham Hospital at the Children's Hospital.
- 9-10 a m Dysmenorrhea. Dr L E Hanes. Joseph H Pratt Diagnostic Hospital.

8 p.m. The Development of Autonomy in Spontaneous Rabbit Tumors. Dr. Harry S. N. Greene. New England Pathological Society. Peter Bent Brigham Hospital.

FRIDAY, NOVEMBER 22

- *9-10 a.m. The Formation of Biliary Calculi Dr Leopold Lichtwitz Joseph H Pratt Diagnostic Hospital
- *12 m Certain Aspects of Nephritis Dr Lichtwitz Joseph H Pratt Diagnostic Hospital.

SATURDAY, NOVEMBER 23

- *9-10 a.m. Hospital case presentation Dr S J Thinnhauser Joseph H. Pratt Diagnostic Hospital.

*Open to the medical profession.

NOVEMBER 15 — Massachusetts Society for Mental Hygiene. Page 648, issue of October 17.

NOVEMBER 15 and 22 — Thomas William Salmon Memorial Lectures Page 692, issue of October 24.

NOVEMBER 22 — Salem Tumor Clinic. Page 831.

DECEMBER 8-11 — American Academy of Dermatology and Syphilology Page 831.

DECEMBER 10 — New England Society of Anesthesiology. Page 743, issue of October 31.

DECEMBER 12 — Pentucket Association of Physicians Page 263, issue of August 15.

DECEMBER 27-29 — National Convention of the Association of Medical Students, Boston.

JANUARY 4, 1941 — American Board of Obstetrics and Gynecology Page 787.

MARCH 8 — American Board of Ophthalmology. Page 201, issue of August 1.

APRIL 21-25 — American College of Physicians. Page 1065, issue of June 20.

MAY 21, 22 — Massachusetts Medical Society, Boston.

JUNE 2-6 — American Medical Association. Cleveland, Ohio.

DISTRICT MEDICAL SOCIETIES

ESSEX SOUTH

DECEMBER 4-MAY 14 — Page 831.

FRANKLIN

JANUARY 14.

MARCH 11.

MAY 13.

Meetings will be held at 11 a.m. at the Franklin County Hospital, Greenfield.

SUFFOLK

JANUARY 29 — Page 604, issue of October 10.

APRIL 30 — Page 604, issue of October 10

WORCESTER

DECEMBER 11 — St. Vincent Hospital, Worcester.

JANUARY 8, 1941 — Worcester City Hospital, Worcester.

FEBRUARY 12 — Worcester State Hospital, Worcester.

MARCH 12 — Memorial Hospital, Worcester.

APRIL 9 — Hahnemann Hospital, Worcester.

Supper at 6:30 p.m. followed by a business meeting and scientific program.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Bone Graft Surgery in Disease, Injury and Deformity. By Fred H. Albee, M.D., LL.D., Sc.D., F.I.C.S.; president, International College of Surgeons; past president, American Orthopedic Association; chairman, Rehabilitation Commission of the State of New Jersey. Assisted by Alexander Kushner, M.D., B.Sc. 4°, cloth, 403 pp., with

297 illustrations. New York: D. Appleton-Century Company, Incorporated, 1940. \$7.50.

The Doctor and His Patients: The American domestic scene as viewed by the family doctor. By Arthur E. Hertzler, M.D. 8°, cloth, 316 pp. New York: Harper & Brothers, 1940. \$2.75.

Public Health Administration in the United States. By Wilson G. Smillie, A.B., M.D., Dr.P.H., professor of public health and preventive medicine, Cornell University Medical College, New York City. Second edition. 8°, cloth, 553 pp., with 22 figures and 9 plates. New York: Macmillan Company, 1940. \$3.75.

Edinburgh Post-Graduate Lectures in Medicine. Vol. I. 8°, cloth, 513 pp., with 110 figures, 32 tables and 11 charts. Edinburgh: Oliver and Boyd, 1940. \$2.10.

Holt's Diseases of Infancy and Childhood: A textbook for the use of students and practitioners. By the late L. Emmett Holt, M.D., and John Howland, M.D. Revised by L. Emmett Holt, Jr., M.D., associate professor of pediatrics, Johns Hopkins University School of Medicine, and associate pediatrician, Harriet Lane Home, Johns Hopkins Hospital, Baltimore, and Rustin McIntosh, M.D., Carpenter Professor of Pediatrics, Columbia University College of Physicians and Surgeons, and director of the Pediatric Service, Babies Hospital, New York City. Eleven edition. 4°, cloth, 1421 pp., with 262 illustrations and 8 plates. New York: D. Appleton-Century Company Inc., 1940. \$10.00.

The Chronicle of Crichton Royal (1833-1936): Being the story of a famous mental hospital during its first century and illustrating the evolution of the hospital care and treatment of mental invalids in Scotland. By Charles Cromhall Easterbrook, M.A., M.D., F.R.C.P.E., physician superintendent, 1908-1937. With a foreword, "Some Early Crichton Memories," by the late Sir James Crichton Browne, M.D., LL.D., F.R.S. 4°, cloth, 663 pp., with 103 illustrations and 1 map. Dumfries, Scotland: Courier Press, 1940. \$5.00.

BOOK REVIEWS

Specialties in Medical Practice. Volumes I and II. By Edgar Van Nuys Allen, M.D. With a foreword by Donald C. Balfour. 4°, cloth; Volume I, 441 pp., with 33 illustrations, and Volume II, 934 pp., with 21 illustrations. New York: Thomas Nelson and Sons, 1940. \$25.00 (set)

Medical books appear in bewilderingly rapid succession monographs for the most discriminating; textbooks for the ordinary student or casual reader; books on special subjects flung as bait to the general practitioner but often of chief use to the specialist; medical or surgical systems loose-leaf or solid, designed to present in black and white the best contemporaneous medical opinion on any topic.

The various systems of medicine or surgery are always difficult to review, for whether in loose-leaf or other form they are a good deal alike,—well printed, handsomely bound and often prettily illustrated. What makes one better than another is the adroitness that the editor-in-chief displays in harnessing together a competent team of writers on the subjects he wishes to elucidate.

Specialties in Medical Practice is an admirable work. It is introduced in what has come to be the traditional manner for any new effort: "The total knowledge accumulated in the practice of medicine far exceeds the capacity of any one physician to acquire it." To meet this generality, the two volumes now in print present in more

graphic form the fields of ophthalmology, diseases of the ear, nose and throat, neurology, psychiatry, vitamins allrgy, orthopedic surgery, obstetrics and gynecology, endocrinology, urology and proctology. The section on dermatology and syphilology is in preparation.

Dr. Allen, the editor in chief, has done his work contently. He has selected for his writers men of reputation, well schooled in the art of writing and chosen impartially from scattered areas all over the country. The format is agreeable to the eye and the illustrations and tables in the various sections are easily comprehensible. Though the cost is high, it is probably not unreasonable for a work of such character. The object has been to describe each specialty so as to make it seem part of general practice, and to give the general practitioner something readable about the various specialties from which he can acquire practical information when in the course of his daily work he encounters a problem on which he needs help.

To those who like systems with which to keep abreast of the times, the book will prove helpful. Those who prefer to read individual works will not purchase it. Owing to buy half a dozen books on subjects that are interesting rather than to invest such a large sum in a literary venture. As systems of medicine go, however, this one is excellent.

Asthma and the General Practitioner. By James Adam, A.M.D., F.R.F.P.S.G., with a foreword by James H. Hilde, O.H. Mavor, M.D. 8th, cloth, 157 pp. Baltimore: Williams & Wilkins Co., 1939. \$2.00.

In his foreword, Dr. Bridie discusses organized research with contemptuous irony. He describes the author as 'a man who can think for himself.' In this all volume, there are so many statements that vary from the mildly questionable to the completely incorrect that it would be difficult to list them all. The following are fair examples of the book's intellectual level:

An eosinophilia means the presence of foreign or ill-split protein'—in short—a dirty blood. Adrenalin is apt—when habitually used—to aggravate the disease and even make it incurable. The aspirin sensitive type seems to have a struggle to maintain the normal pH of 7.4, and a small dose of acetylsalicylic acid rapidly absorbed may suffice to tip the balance of the respiratory system. It is remarkable that Nature has chosen the lungs for throwing off ill-split protein with which the liver has failed to deal. The warm air of the paranasal sinuses is drawn upon during violent effort. Whiteness of the hair, Graves' Disease, myxoedema, I have known to result from mental shock. High heels lead to nasal congestion and catarrh. However, flat feet, corns, bunions, all hinder improvement and prevent cure.

Sunshine breeds vitamin D in the body. No asthmatic makes progress who has flatulence (gastric or intestinal), or has constipation. Colonic douching may subdue the asthma quicker than any other treatment. Many an asthmatic has said that he has had to give up golf because of wheeze. Many have found by perseverance that it cures the wheeze. It is one of the best medicines for asthma. The darkness around [sic] the eyes is not due to cosmetics but to other dirt internally generated and to defective adrenal function. Against inhalants a strong mixed vaccine [sic] is usually supplied.

It appears that the author can ill afford his bellicose attitude toward organized research. Scientific training would have taught him the correct meanings of the words

breed and vaccine. Common sense should tell him that high heels are certainly not a common cause of nasal congestion and catarrh, nor golf the best medicine for asthma.

Manual of Fractures, Dislocations and Epiphyseal Separations. By Harry C. W. S. de Brun, M.D. 468 pp. 8th, cloth. Chicago: The Year Book Publishers, Inc., 1939. \$3.00.

Drawing from his long experience in war and civilian practice and from his teaching of bone surgery, the author has succeeded admirably in preparing an authoritative and concise work. He has divided the presentation into four parts. Part I is devoted to general considerations, general principles and treatment, anesthesia and aftercare. Parts II and III discuss specific fractures and dislocations. The usual and some of the more unusual types are described. This section presents clearly and tersely one, and sometimes more than one, method of closed reduction, and also the principles of open reduction. The scope of the work is greatly enhanced by Part IV, which is designed to aid the fracture surgeon in organizing and maintaining a hospital group, clinic or industrial dressing room. Here in are set forth the preparation and uses of plaster of Paris, the equipment, the fracture records and the method of rating end results employed at the Massachusetts General Hospital. Dr. Kovacs has contributed a practical chapter on physical therapy, and Dr. Kaplan on positioning exposure and interpretation of roentgenograms. There is a good eight page double-column index.

The illustrations are carefully selected and clearly reproduced. The typography and paper are excellent. The work was of especial interest to the reviewer, who heartily recommends it to students, practitioners, and hospital and industrial libraries.

Clinique et Physopathologie des Maladies Coeliques. By Robert Dubois. 8th, paper, 344 pp. Paris: Masson et Cie, 1939. 80 Fr. fr.

This monograph contains a rather detailed discussion of the various aspects of celiac disease, which include the so-called idiopathic steatorrhea and nontropical sprue. The clinical aspects are considered in great detail as are the alterations in metabolism. The latter are based on extensive biochemical studies by the author, and many protocols are included. He emphasizes the defective absorption of betosylvine, which was found in all the cases that he studied. The autopsy findings in one of his six cases are also recorded. There is a chapter summarizing ideas on etiology and pathogenesis and another on therapy. Like most recent French monographs it is presented in a simple style and is well arranged. It contains a useful bibliography.

The Participation of Medical Social Workers in the Teaching of Medical Students. By Harriet M. Bartlett. 8th, cloth, 68 pp. Chicago: American Association of Medical Social Workers, 1939. \$1.50.

Medical social service has become firmly established as an essential part of the modern hospital, especially the metropolitan hospital with a large outpatient department. Its primary aim, although many other worthwhile functions have become associated with this service, is to carry out properly in the home the hygienic directions given in the hospital as pointed out by Osler many years ago.

Now as indicated in the author's report, a complicated structure has grown up giving a professional standard to medical social service work. How much of this should

be taught to the medical student, as part of the curriculum of a modern medical school? Certainly, no well-trained physician should be ignorant of the subject, and some way must be found to impart this knowledge to him. The movement is under way, and this report gives the essentials needed to carry out the program. How to find a place for the teaching of medical social service in an already overcrowded curriculum is by no means an easy problem for deans and administrators to solve. A program, at least, is prepared, and this book gives an outline of what should be done.

Periodontal Diseases: Diagnosis and treatment. By Arthur H. Merritt, D.D.S., M.S., F.A.C.D., F.A.A.P. Second edition. 8°, cloth, 205 pp., with 44 illustrations and 1 chart. New York: Macmillan Company, 1939. \$3.50.

The subject of periodontal diseases is one that should concern not only the dental practitioner but also the practitioner of medicine in order that he may have a clear conception of the diseases of the gums and related structures. This small volume, attempting to classify the existing knowledge of periodontal diseases, does it very well, but altogether too briefly, especially considered from the pathological viewpoint.

The relation of periodontal diseases to systemic conditions is mentioned, as are lesions of the gums due to drugs; however, the discussion of specific causes is rather limited. There is practically no reference to avitaminosis or allergic reactions. Gingival hypoplasia due to Dilantin Sodium, which has recently become a very common condition in epileptics, is not mentioned.

Without being too critical, one can consider this edition as a useful contribution to our present knowledge of periodontal diseases. Further research will be helpful in classifying many of these pathologic conditions involving the gums. The bibliography is fairly complete, but there is almost a complete absence of foreign references.

Heil Hunger: Health under Hitler. By Dr. Martin Gumpert. Translated from the German by Maurice Samuel. 8°, cloth, 128 pp. New York: Alliance Book Corporation, 1940. \$1.75.

Utilizing only, as he says, data from official Nazi publications and German technical magazines, Dr. Gumpert tries to show that Herr Hitler has failed to lead his people into the promised land of better health and physical fitness. On the contrary, there has been a notable weakening of the national constitution. And perhaps there are delayed effects. Nevertheless, one is left far from convinced. Certainly the German military material has given no sign of decrepitude. If German man power is weak then *Der Fuehrer* and the German high command must be credited with a near miracle.

Diabetes: Practical suggestions for doctor and patient. By Edward L. Bortz, A.B., M.D., and others, with a foreword by George Morris Piersol, B.S., M.D. Second edition, revised and enlarged. 8°, cloth, 296 pp., with 15 illustrations. Philadelphia: F. A. Davis Company, 1940. \$2.50.

In this second edition, the author has rewritten the chapter on insulin, emphasizing the use of protamine zinc insulin for all patients beginning the use of insulin and the employment of crystalline insulin when a supplementary dose is needed. The simple and nontechnical style befits its purpose as a manual for the instruction of patients.

The Pathology of Internal Diseases. By William Boyd, M.D., M.C.C.P. (Edin.), F.R.C.P. (Lond.). Third edition. 8°, cloth, 874 pp., with 353 illustrations and 4 colored plates. Philadelphia: Lea & Febiger, 1940. \$10.00.

For some years there has been a preponderant trend toward a physiologic approach to medicine, manifested by the neogenesis of a literature based on the conception of clinical medicine as a perversion of normal function. This replacement of pathologic anatomy by pathologic physiology has been justified to the extent that a clearer conception of the mechanism of disease became available. A background of knowledge of gross and microscopic pathology is, however, necessary to round out a true understanding of disease processes.

The author has attempted a fusion of these fields with successful results, as may be attested by the use of his book as a standard text in many schools. A wide field is covered, and, as is necessary in a book of this size, certain limitations are self-imposed and certain omissions are found. One finds compensation in a well-arranged bibliography for further study.

In future editions one will undoubtedly find more of the rapidly accumulating data on vitamin deficiencies and hormonal changes. Some of the new sections introduced by the author cover cardiac hypertrophy, Fiedler's myocarditis, intimal coronary hemorrhage, Vitamin K, reticuloses, equine encephalomyelitis and extrarenal urem.

Fetal and Neonatal Death. By Edith L. Potter, M. Ph.D., and Fred L. Adair, M.D. 12°, cloth, 207 pp., with 31 illustrations. Chicago: University of Chicago Press, 1940. \$1.50.

This book is aimed to furnish descriptive material concerning the technic of autopsy examination of the fetal and newborn infant. This is well done. The authors proceed further to a discussion of the diseases, general and special, productive of fetal and neonatal deaths. In this country there are annually about 75,000 recorded stillbirths and 142,500 fetal and neonatal deaths. A number of the deaths—according to some estimates as many as a third—are preventable. Exactly how they are to be prevented this treatise does not show. But it may start people thinking, and it does furnish some data which may lead to further investigations.

Cancer: A handbook for physicians. Prepared by the Tumor Committee of the Connecticut State Medical Society. 8°, paper, 193 pp., with 5 charts. Hartford: Connecticut State Department of Health, 1939.

This volume is a useful compendium. The first chapter presents a detailed study of the incidence of cancer mortality and shows the trend toward increase in the disease in Connecticut. Unfortunately, the statistical graphs do not extend beyond 1935.

There is a clear exposition of the cancer organization in Connecticut. The book then goes on to a general discussion of cancer in which etiology, pathogenesis, pathologic diagnosis and prevention are considered. Emphasis is laid on the annual physical examination as a means of detecting early carcinoma. Chapters on the general uses of surgery, x-ray and radium for treatment of cancer and the value of biopsy are followed by a group of thirteen chapters covering the tumors as they appear in the various sites. Three chapters are then devoted to the treatment of inoperable cancer. The opinions expressed are in accord with those generally held.

The New England Journal of Medicine

Copyright, 1940, by the Massachusetts Medical Society

VOLUME 223

NOVEMBER 21, 1940

NUMBER 21

THE ORGANIZATION OF A PSYCHIATRIC CLINIC IN THE OUTPATIENT DEPARTMENT OF A GENERAL HOSPITAL*

ROBERT FLEMING, M.D.,† GAYLORD P. COON, M.D.,‡ A. W. CONTRATTO, M.D.,§ JOHN M. FLYNN, M.D.,||
CHARLES R. ATWELL, M.A.,|| AND GERNA S. WALKER, A.B.

BOSTON

ON OCTOBER 13, 1936, under the inspiration of Dr. Henry A. Christian, a psychiatric clinic was opened in the Out-Door Department of the Peter Bent Brigham Hospital, which met one half day each week, and to which ambulatory patients were to be referred from other clinics in the hospital. In the following three years 443 patients made a total of 2551 visits to the clinic—an average of slightly under six visits per patient. This represents roughly 2 per cent of all the new patients (1 per cent of the visits) who went to the Out-Door Department during the three-year period. During the first few months it became apparent that a single half day per week was inadequate to handle the volume of referred cases, and accordingly in January, 1937, another half-day period was added and reserved primarily for adolescent cases and for problems of alcoholism; subsequently, with increasing professional personnel, it was possible to add psychiatric sub-clinics, held for half-day periods, until at the end of the first three years four physicians and one psychologist were spending a total of six half days each week dealing with psychiatric patients under the auspices of the Psychiatric Clinic.

It was gratifying to feel from the start an interested and cordial attitude, especially on the part of the medical house officers and the junior members of the associate staff of the hospital; some of the latter, perhaps because of an appreciation, often deviously acquired, of the importance of emotional and psychological elements in disease, evinced

an eagerness to take part in the enterprise as a means of learning more about the role these forces play. Two factors led to the utilization in the clinic—at first reluctantly and of necessity, later by choice—of nonpsychiatrically trained personnel. First, the problem which the clinic had to face almost from the beginning was that of too many patients, so that it became imperative to increase the professional staff in order to avoid the piling up of an absurdly long waiting list; secondly, at the time only nonpsychiatrically trained volunteers were available. Actually this worked out rather well, and in a number of ways it has been an advantage to have certain types of psychiatric outpatients handled by physicians who are interested in them, and yet devoid of many of the prejudices and orthodox attitudes of both the conventionally trained psychiatrist and the organically minded internist. The internist usually does not know much about handling psychotic patients, but such patients do not constitute a major problem in the psychiatric clinic of a general hospital—about 10 per cent of the total cases seen. However, the internist is often much more adept and resourceful in dealing with a patient with physical symptoms—even though they are emotionally determined—than is the ordinary psychiatrist.

Furthermore, the utilization of interested internists has been made more practicable in our organization by having each patient referred to the Psychiatric Clinic first pass through a central or clearing-house clinic. There the patient is seen by a psychiatrist, a history is taken, a tentative diagnosis is made, and plans for treatment or disposition are formulated. At this initial visit, any one of several possible courses may be followed, depending on the type of case. The problem may be settled effectively in a single interview. If the patient is psychotic he may be referred to the Bos-

*From the Medical Service, Peter Bent Brigham Hospital.

†Instructor in psychiatry, Harvard Medical School; junior associate in medicine, Peter Bent Brigham Hospital.

‡Associate in psychiatry, Harvard Medical School; chief medical officer, Boston Psychopathic Hospital.

§Assistant in medicine, Harvard Medical School; junior associate in medicine, Peter Bent Brigham Hospital.

||Associate in medicine, Peter Bent Brigham Hospital.

||Instructor in psychology, Harvard Medical School; psychologist, Boston Psychopathic Hospital.

ton Psychopathic Hospital* directly, or arrangements may be made for him to be followed in the Psychiatric Clinic. He may be referred to some other clinic (surgical, arthritic, gynecological and so forth) of the Out-Door Department for an opinion on some special aspect of the case, or to the psychologist for special psychological tests. He may be sent into the hospital for a more intensive study than is possible in the Out-Door Department; or suitable cases may be referred to any of the special psychiatric subclinics for further handling. The whole organization has been characterized by great flexibility within a well-defined framework, permitting the orderly focusing of the diagnostic and therapeutic resources of the entire hospital and its staff on the needs of the individual psychiatric outpatient.

The idea of special psychiatric subclinics has worked out quite satisfactorily from a number of viewpoints. It is of advantage to a patient to be in the hands of a physician who is especially interested in his particular problem; it is likewise of advantage to a physician to be able to concentrate, simultaneously and exclusively, on a group of selected patients all of whom fall into the same general category of clinical picture or problem. One of the special clinics (A.W.C.'s) has been devoted in the main to problems arising out of the social and cultural assimilation of foreign-born patients, particularly those from Italy and other Mediterranean countries. Another of us (G.P.C.) has been working with cases of classic hysteria,—apparently less common now than it was fifty years ago,—which often show striking conversion symptoms and which present special problems of management in an outpatient clinic. To a third special clinic (J.M.F.'s) have been referred two types of cases: first, those in whom a conflict between religious belief and biological drives seems to form the center of the problem; and secondly, psychoneurotic patients in whom the symptomatology has been largely limited to the gastrointestinal tract.

It was not until the Psychiatric Clinic had been in existence for nine months that a trained psychiatric social worker (G.S.W.) was added to its personnel on a half-time basis; previously the facilities of the regular Social Service Department had been used when necessary. At the end of its third year the clinic still has a half-time social worker, who is assisted one morning a week by a volunteer clinic manager.† The varied administrative de-

tails of clinic management have of necessity been assumed by the social worker, in addition to an initial interview with each patient admitted to the Psychiatric Clinic, and to the psychiatric case work which is her usual function.

In the social worker's interview with each new patient before the latter is seen by the psychiatrist, a fairly complete social history has been taken. Contrary to the fears of some persons interested in the clinic, this interview and history have, so far as we can ascertain, in no case antagonized the patient. Nor, we believe, has it made the establishment of a sound rapport between psychiatrist and patient more difficult. It has in most cases made for a feeling of friendliness and confidence toward the clinic as a unit. It has proved of value to the psychiatrist, to the social worker and to the patient. The history has given the psychiatrist details of the patient's heritage and social background useful to him in evaluating the psychiatric condition, details which he himself has little time for eliciting during the operation of a busy clinic. The knowledge of each patient which the social worker gains makes for efficiency in handling problems referred to her by the psychiatrist during the course of treatment. A detailed and time-consuming interview at the time of referral is often avoided since the basic information is already on record. More important than this, perhaps, is the fact that when a referral is made the patient believes that he is being sent to someone who already knows him and who has a friendly attitude toward him.

A patient referred to a psychiatric clinic often keeps his first appointment with a good deal of trepidation. To him this initial interview frequently provides a means of gaining some understanding of the clinic, of obtaining answers to puzzling questions and of assuaging some of his fears.

The psychiatric case work in the clinic has fallen into both the short-service and intensive group. It has, however, been possible for the social worker to carry only a small number of cases requiring intensive social treatment, because of her multiple duties in connection with the clinic and the lack of time in which to do them.

The diagnoses in the 443 cases seen in the clinic during the three-year period are shown in Table 1, in which many of the difficulties of psychiatric diagnosis are reflected; chief of these is the lack at the present time of any sufficiently comprehensive basis for making etiologic diagnoses. With a few notable exceptions (syphilis, post-traumatic conditions), the diagnostician is forced to use the unsatisfactory expedient of grouping together cases the symptomatology of which seems similar, even

*It has always been an indispensable advantage in the organizing and functioning of the Psychiatric Clinic to have the frequent and cordial counsel of various members of the staff of the Boston Psychopathic Hospital, notably Dr. C. Macfie Campbell, Dr. F. L. Wells and Miss Esther M. Cook, and easy access to the facilities of that hospital, especially in handling psychotic patients.

†The staff gratefully acknowledges the efficient assistance of Mrs. Richard D. Gerould in this capacity.

though he frequently suspects that different symptoms may arise by similar etiologic means, and vice versa. The result of this "system" is often a comforting appearance of orderliness, which is, however, deceptive, and serves more to obscure lack of knowledge than to express orderly relations ac-

TABLE 1. *Diagnoses.*

DIAGNOSIS	MEN	WOMEN	TOTAL	PER CENT
Psychoneurosis				
Anxiety type	60	113	173	39.0
Hysterical type	8	30	38	8.6
Unspecified type	1	9	10	2.3
Psychosis				
Schizophrenia	8	3	11	2.5
Manic-depressive psychosis	2	12	14	3.1
Involutional melancholia	1	2	3	0.7
Psychosis with cerebral arteriosclerosis	0	2	2	0.5
Psychosis with epilepsy	0	1	1	0.2
Paranoid condition	1	2	3	0.7
Psychosis, undiagnosed	1	7	8	1.8
Mental deficiency	6	5	11	2.4
Epilepsy				
Idiopathic	1	2	3	0.7
Post traumatic	0	1	1	0.2
Chronic alcoholism	30	3	33	7.4
Chronic malnutrition	1	0	1	0.2
Drug addiction (morphine)	1	0	1	0.2
Social maladjustment	6	4	10	2.3
Frauds, nocturnal	2	0	2	0.5
Stammering of unknown cause	2	0	2	0.5
Psychopathic personality	13	15	28	6.3
Syphilis of the central nervous system				
Tabes dorsalis	3	0	3	0.7
Paralysis	0	0	0	0
Other types	1	1	2	0.5
Cerebrovascular disease, with out psychosis	3	0	3	0.7
Postencephalitic Parkinsonism	1	1	2	0.5
Combined system disease	0	1	1	0.2
Sydenham's chorea	1	0	1	0.2
Ménière's syndrome	0	1	1	0.2
Spasmodic torticollis	0	2	2	0.5
Cortical atrophy (hydrocephalus)	0	1	1	0.2
Subdural hematoma	0	1	1	0.2
Essential hypertension	0	1	1	0.2
Impotence functional	1	0	1	0.2
Dysmenorrhea of unknown cause	0	2	2	0.5
Menopausal syndrome	0	1	1	0.2
Dyspareunia functional	0	2	2	0.5
Headache of unknown cause	4	1	5	1.1
Tinnitus of unknown cause	0	2	2	0.5
Hyperinsulinism (adenoma of pancreas)	1	0	1	0.2
No psychiatric condition	1	7	8	1.8
Undiagnosed (neurologic condition)	0	1	1	0.2
Undiagnosed	18	29	47	10.6
Totals	178	265	443	

tion. The current tendency of most diagnosticians is to make the diagnosis of psychoneurosis by exclusion: whenever there has been a failure to demonstrate organic disease, the case becomes *ipso facto* psychoneurotic. In contrast to this usage, it is our experience that it is frequently possible to make a positive and valid diagnosis of psychoneurosis even in the presence of organic disease; likewise, after careful study of a case one is frequently able to state positively that no psychoneurosis exists. As an example, the presence or absence of pain is often a helpful criterion: one gains

TABLE 2. *Age Distribution.*

AGE	MEN	WOMEN	TOTAL
12-19	24	29	53
20-29	37	54	91
30-39	49	73	122
40-49	40	70	110
50-59	25	28	53
60-69	2	11	13
70 and over	1	0	1
Totals	178	265	443

the impression that pain is rarely a primary psychoneurotic symptom, even in conversion hysteria, and that where it is prominent in the symptomatology, the presumption is strongly in favor of an organic lesion. For the purposes of this report two main types of psychoneuroses have been distinguished, the anxiety type (including, as generically related, obsessional, hypochondriacal and

TABLE 3. *Marital Status.*

STATUS	MEN	WOMEN	TOTAL
Married	97	140	237
Single	70	92	162
Widowed	4	19	23
Divorced	5	13	18
Separated	2	1	3
Totals	178	265	443

tually existing. It is interesting, however, to obtain a bird's-eye view of the incidence and diversity of the various clinical pictures encountered in the psychiatric clinic of a small medical outpatient department.

As might have been expected, considering the source of the clinical material, the psychoneuroses comprised the largest single diagnostic group, with 221 cases in all, or half the total number seen. The term "psychoneurotic" often becomes merely a convenient epithet among physicians, and as such more descriptive of the physician's attitude toward his patient than of the latter's real medical condi-

tion. The current tendency of most diagnosticians is to make the diagnosis of psychoneurosis by exclusion: whenever there has been a failure to demonstrate organic disease, the case becomes *ipso facto* psychoneurotic. In contrast to this usage, it is our experience that it is frequently possible to make a positive and valid diagnosis of psychoneurosis even in the presence of organic disease; likewise, after careful study of a case one is frequently able to state positively that no psychoneurosis exists. As an example, the presence or absence of pain is often a helpful criterion: one gains

*The basis for this nosological concept will be developed in detail in another paper (Fleming R; unpublished data).

The possibilities for and limitations of utilizing the facilities of the outpatient department of a general hospital for the treatment of chronic alco-

TABLE 4. *Occupational History.*

OCCUPATION	MEN	WOMEN	TOTAL
Arts	5	4	9
Clerical work	12	21	33
Factory work	12	8	20
Government service	1	0	1
Housewife	0	146	146
Laborer	20	0	20
Building trades	34	0	34
Personal service	31	34	65
Professions	7	3	10
Salesman	24	15	39
Sewing trades	5	8	13
Student	20	22	42
None	1	0	1
Unknown	6	4	10
Totals	178	265	443

holism have been of particular interest to one of us (R. F.), and a special subclinic has been established for dealing with this problem. Although

TABLE 5. *Distribution of Races and Nationalities.*

RACE OR NATIONALITY	MEN	WOMEN	TOTAL
American	36	50	86
Armenian	0	2	2
Armenian American	0	1	1
Assyrian American	1	0	1
Canadian	6	15	21
Canadian American	1	0	1
English	1	1	2
English American	3	1	4
English French American	0	1	1
English Irish American	1	0	1
English Irish Portuguese American	1	0	1
English Norwegian American	0	1	1
English Welsh American	0	1	1
French	0	2	2
French American	1	3	4
French Canadian	1	4	5
French Canadian English American	0	1	1
French Irish American	0	1	1
Finnish American	1	0	1
German	1	2	3
German American	3	8	11
German Irish American	0	2	2
Greek	0	3	3
Indian Scotch Irish	1	0	1
Irish	10	17	27
Irish American	30	32	62
Irish Indian American	0	1	1
Italian	16	19	35
Italian American	4	10	14
Italian French American	2	1	3
Jewish	30	65	95
Jewish Irish American	1	0	1
Leit	1	0	1
Lithuanian	3	2	5
Negro	3	4	7
Norwegian	0	1	1
Norwegian American	1	0	1
Pennsylvania Dutch Irish American	0	1	1
Polish	1	1	2
Polish American	1	2	3
Portuguese American	2	1	3
Portuguese Irish American	1	1	2
Scotch	3	0	3
Scotch American	3	1	4
Scotch Irish	0	1	1
Scotch Irish American	0	1	1
Swedish	2	1	3
Swedish American	2	2	4
Swedish Finnish American	0	1	1
Syrian	1	0	1
Syrian American	1	0	1
Unknown	2	1	3
Totals	178	265	443

the total number of alcoholic patients so far seen in this subclinic is small (30 men and 3 women),

it is already apparent that certain types of alcoholic patients can be successfully treated as ambulatory, it would seem that the drinker who tends to do well in such a setting is often one in whom physical symptoms (due to gastritis, avitaminosis and so forth) are prominent.

The age distribution and marital status of the patients are shown in Tables 2 and 3. It is to be noted that 376 (85 per cent) of them were under fifty years of age. Although the number under twenty was not relatively large (53, or 12 per cent) the importance of this group of young patients as regards response to treatment and the desirability of special facilities to deal with the problems of adolescence is apparent. Where a prolonged contact with a child has been needed the function of the

TABLE 6. *Distribution of Religions.*

RELIGION	MEN	WOMEN	TOTAL
Roman Catholic	76	109	185
Hebrew	31	65	96
Baptist	10	11	21
Congregational	12	15	27
Episcopal	9	12	21
Methodist Episcopal	3	6	9
Methodist	4	8	12
Presbyterian	2	1	3
Lutheran	1	4	5
Swedish Emanuel	1	0	1
Protestant	6	7	13
Greek Orthodox	0	3	3
Assyrian Orthodox	1	0	1
Christian Science	0	1	1
Unitarian	3	1	4
Unity Church of Christ	0	1	1
Universalist	0	1	1
Apostolic	0	1	1
Spiritualism	0	1	1
None	6	4	10
Unknown	13	14	27
Totals	178	265	443

psychiatric clinic has been to place the child in the hands of one of the excellent special agencies already existing in the community (Judge Baker Foundation, New England Home for Little Wanderers, Children's Aid Association, Massachusetts Department of Mental Hygiene clinics and so forth) rather than to attempt to build up a complete but duplicating adolescent clinic. The services of the psychologist (C. R. A.) are particularly helpful in deciding on the disposition and handling of children where questions of intelligence levels, vocational aptitudes and so forth arise.

The occupation, race and religion of the patients are shown in Tables 4, 5 and 6. It was impossible to have a special group of unemployed because of frequent shifting; many patients found employment in the course of their treatment at the clinic, and vice versa. One gains the impression that with a single exception the racial distribution of the population from which the hospital draws its patients is quite accurately reflected in the racial distribution of our cases; the exception is to be found

in the disproportionately large number of Jewish patients, 95 (21 per cent).

The financial rating of the patients, shown in Table 7, gives a good idea of the economic levels from which they are recruited. It is interesting that the largest single group is composed of patients with an A rating, who pay 50 cents a visit,

psychiatric clinic in the out-patient department of a small general hospital are discussed.

To this clinic were referred 443 cases in three years; these patients made an average of about six visits each.

Women outnumbered men by about 3:2. Eighty-five per cent of the patients were under

TABLE 7. *Total Number of Visits and Total Income.*

RATING	MEN			WOMEN			TOTAL		
	NO OF CASES	NO OF VISITS	FEES	NO OF CASES	NO OF VISITS	FEES	NO OF CASES	NO OF VISITS	FEES
A	102	411	\$305 50	165	742	\$371 00	267	1153	\$576 50
B	12	56	14 00	50	212	53 00	62	268	67 00
B x	22	112	16 80	44	149	22 35	66	261	39 15
C	96	427		103	377		199	804	
X	6	35		5	30		11	65	
Totals	238	1041	\$236 30	367	1510	\$446 35	605	2551	\$682 65

These ratings are determined by the economic status of the patient: patients with an A rating pay fifty cents per visit; those with a B rating twenty five cents, those with a B x rating fifteen cents, and those with a C or X rating nothing.

rather than, as might have been expected, the completely indigent. It is also to be noted that the clinic as currently organized can count on an annual income of something over two hundred dollars from the patients themselves.

SUMMARY

Some of the problems of the organization of a

fifty years of age, and 12 per cent were under twenty.

About half the patients (221) were diagnosed as suffering from a form of psychoneurosis, and of these 80 per cent were of the anxiety type.

About 10 per cent of the patients were psychotic, and the question of institutionalization came into consideration in these cases.

CANCER OF THE STOMACH

HOWARD M. CLUTE, M.D.,* AND THOMAS J. ANGLEM, M.D.†

BOSTON

IN THE five years from January 1, 1935, to January 1, 1940, we have examined and treated 68 cases diagnosed preoperatively as cancer of the stomach. A review of our experiences with these cases reveals much that is discouraging, but nevertheless gives reason for at least some optimism. We shall report our analysis of the results of treatment including both ward and private patients, and give our views regarding certain measures that may tend to improve the present, rather depressing, situation.

Until Billroth's first successful gastric resection in 1881, cancer of the stomach was amenable to no known form of treatment, and carried a mortality of 100 per cent. In the years immediately following, little progress was made because few cases reached the surgeon sufficiently early to permit resection. Cancer of the stomach was known clin-

ically only in its advanced stages, and the persistent representation of the disease in textbooks and in medical teaching in terms of the signs and symptoms of its late stages has been one of the serious obstacles in the way of progress toward its control.

A study of the histories in our series indicates that many physicians are still thinking of gastric cancer in terms of its advanced stages: in terms of severe epigastric pain, of a palpable epigastric mass, of coffee-ground vomitus, of severe anemia and extensive weight loss—symptoms and signs that, in the vast majority of cases, mean inoperability and hopeless prognosis. It is apparent that physicians in general are not sufficiently alert to the now well-established fact that there are no early pathognomonic signs or symptoms of gastric cancer. We doubt whether it is recognized that, if early diagnosis is to be established, the disease must be suspected on the basis of symptoms that can be said to be at most vaguely suggestive,

*Professor of surgery, Boston University School of Medicine, surgeon in chief, Massachusetts Memorial Hospitals.

†Second assistant surgeon, Massachusetts Memorial Hospitals.

that is, indigestion, dyspepsia, unexplained weight loss or anemia, however mild, and what Harris¹ calls "stomach consciousness" developing in a patient who has previously been oblivious of his gastric function.

This failure to suspect the possibility of cancer on the basis of early symptoms was the prime cause of delayed diagnosis in our cases, and we were astonished at the number of cases in which the patients were treated medically for months before x-ray studies were even considered. Many were kept under treatment with pills and powders for three months without any suggestion of x-ray study, and some went six months to a year before any attempt was made to learn the cause of the persistent or changing digestive disturbances.

It is not commonly recognized how rapidly cancer of the stomach grows and metastasizes. In our experience are cases with x-ray evidence of apparently small lesions that developed into inoperable growths in two to five months. Obviously, then, an active, aggressive policy of investigating the *cause* of digestive symptoms immediately after onset is the first necessary step if the salvage from this disease is to be increased.

Not all the onus for the delay in the detection of gastric cancer, however, can be laid on the shoulders of the physician. The x-ray diagnostician and also the surgeon are not infrequently responsible for considerable procrastination.

A definite factor, of great practical importance, which militates against the establishment of early diagnosis is the high cost of adequate x-ray studies. We have discussed this matter with a number of excellent physicians engaged in general practice, and it has been their common experience that gastrointestinal x-ray examination, advised in cases of digestive disorders of mild or moderate degree, is frequently refused by the patient because of the expense involved. Whether or not it is feasible for roentgenologists to provide adequate gastrointestinal examinations for a fee more within the reach of the average patient is difficult to say. Certainly from the standpoint of both surgeon and patient some step in this direction is imperative if the mortality from cancer of the stomach is to be reduced.

In the hands of the expert roentgenologist, the presence or absence of gastric cancer is generally regarded as being demonstrable with an accuracy of 90 or 95 per cent. In spite of what are now regarded as adequate diagnostic methods, there remain, nevertheless, cases in which the roentgenological opinion is not borne out by the findings at operation. There were, for example, 5 cases in this group in which the operative findings did not

entirely confirm the x-ray diagnosis. In 3 cases x-ray studies showed the typical deformity of gastric cancer and yet at operation no lesion was found in the stomach. Cases with exaggerated gastric peristalsis and spasm often confuse the roentgenologist, and the diagnosis can often be settled only by exploratory laparotomy. In all the above-mentioned cases there were other findings suggestive of cancer. Even though these are equivocal, one would hesitate to disregard repeatedly positive x-ray studies. In 1 case a prepyloric lesion thought on x-ray examination to be cancer proved to be a fibroma of the stomach wall. Resection was carried out because the benign nature of the process was not recognizable until the specimen was removed. In the fifth case there was much difference of opinion between several members of the x-ray and clinical staffs as to the nature of the small prepyloric ulcer that was visible in the film. Because of this uncertainty a subtotal gastrectomy was performed. A small ulcer was found proximal to the pylorus on the lesser curvature of the stomach. Sections of this ulcer were reviewed by three Boston pathologists, all of whom agreed that it was a precancerous lesion — not yet fully malignant.

Such a case as the last cannot be considered as a failure in x-ray diagnosis. On the contrary, on examination of the specimen it was astonishing that such a tiny lesion could be seen by x-ray. It is clear, as shown in several other cases in our series, that the inability of the x-ray diagnostician to make a definite differential diagnosis between ulcer and cancer may easily lead to undesirable delay in instituting proper therapeutic measures. In a recent case, for example, the roentgenologist reported a large ulcerating lesion as probable cancer and suggested that the patient return in three weeks for re-examination; operation disclosed a hopeless cancer with widespread metastases. This practice is by no means unusual with both internists and roentgenologists. The objective, of course, is accuracy in diagnosis, but such a diagnosis attained by defying the progress of the disease is often too dearly bought to justify the practice. When the x-ray picture is at all suggestive of cancer, immediate surgery is preferable to delay and repeated x-ray examination.

The value of accurate preoperative diagnosis cannot be too much emphasized, and we do not wish to urge hasty exploration. Long delays must be avoided. Obviously, it is a very grave matter to subject to gastric resection patients with benign lesions amenable to operative procedures of lesser magnitude or to purely medical treatment. Every reasonable aid must be employed to determine the diagnosis preoperatively. It is well known that

the surgeon is often unable to determine at the operating table whether an early gastric lesion is benign or malignant. We have removed lesions that appeared to be benign and found them malignant; and conversely we have resected lesions that appeared to be malignant but were benign.

In many cases of suspected gastric cancer the diagnosis is definitely established by x-ray examination. In other cases the findings are equivocal, and the roentgenologist is either unwilling to commit himself or is led into error. We are convinced that one of the commonest causes of such error is that examination is carried out on an organ that has long been partially obstructed, and that accurate delineation of the lesion is impossible because of the presence of fluid and food particles in the stomach or because of edema and thickening of the gastric wall and hypertrophy of the gastric rugae. In such cases satisfactory x-ray studies can often be carried out only after three or four days of decompression of the obstructed organ by intermittent or continuous gastric drainage. Not infrequently, however, even when the first x-ray studies are made under favorable circumstances, it is still impossible to arrive at a definite diagnosis. In such cases we are accustomed to keep the patient on a careful ulcer diet, with Sippy powders, for five or ten days, after which the x-ray studies are repeated. Persistence of pain, of the defect, without evidence of healing, and of occult blood in the stools constitutes strong presumptive evidence of cancer. The converse, it is essential to emphasize, is not necessarily true. Temporary amelioration of symptoms and temporary diminution in the size of a cancerous ulceration often occur after medical treatment, and are sources of error which may lead to delay in establishing the true diagnosis.

The perfection of gastroscopic technics by Schindler and others provides another diagnostic method that is most useful in cases where the diagnosis remains uncertain after x-ray examination; gastroscopy should be carried out in all such cases. In our experience, however, gastroscopy is by no means an innocuous procedure, and serious accidents and fatalities may follow its use. We have seen esophageal perforations with fatal termination in 2 cases referred elsewhere for gastroscopic study. In neither case was the lesion malignant.

It is in these occasional uncertain cases that the surgeon may be responsible for too long a delay before resecting the stomach. When the internist and roentgenologist are in doubt, it is at times very difficult for the surgeon to insist on resection. The uncertainty of the diagnosis makes him hesitate to subject the patient to the unavoidable yet considerable risk that this procedure involves.

However, it is in such cases that he has his best chance to perform a safe resection. The knowledge that subtotal gastrectomy carries an operative mortality of 10 to 20 per cent should not lead him to delay operation. In this series, the 4 postoperative deaths in a group of 27 resections all occurred in cases with very extensive lesions. Any one of them might very reasonably have been rejected as of doubtful operability. We have every reason to believe that gastric cancer can be resected with a very low mortality rate if early cases are selected.

Nineteen of the 68 cases (29 per cent) were explored and found to be inoperable. One patient in this group died postoperatively of cardiac failure and pulmonary edema. Eleven other cases were not suitable even for exploration, and in 8 only palliative operative procedures were possible. Of 68 cases in the series, 38, or more than half, were hopeless from the point of view of operative curability when first seen. It is apparent without further comment that the early diagnosis of gastric cancer is still far from satisfactory.

Although one may be inclined to criticize the failure of physicians to refer cases of gastric cancer for surgery earlier in the course of the disease, the surgeon who must subject over a quarter of his patients to exploratory laparotomy to establish inoperability also leaves himself open to some criticism.

The question of accuracy of diagnosis should embrace the separation not only of malignant from nonmalignant lesions, but also that of operable from inoperable cases. The decision as to operability in any given case is often difficult, however, and since this is a matter of extreme urgency, it should be decided only after the most careful search for evidence of advanced disease. These patients fall very largely in the older age group, and are oftener than not seriously debilitated by their disease. The ratio of operative mortality from simple exploration is high—about 5 per cent. Obviously, it is entirely unwarranted to subject these patients to so great a risk of primary mortality if it is at all possible to establish inoperability by clinical methods.

The criteria that indicate inoperability are well known. In brief these are the presence of a large fixed mass; ascites; involvement of the cardiac opening of the stomach by the lesion; a roentgenogram showing the stomach drawn close to the spine or to the right of it (suggested by Allen²); a large nodular liver (we have several times found only the left lobe of the liver palpably enlarged); and the presence of distant metastases.

The search for distant metastases should in all cases include the most painstaking palpation of the supraclavicular areas.—particularly the left.

which is more often affected,—for the presence of involved lymph nodes, the Virchow's or sentinel nodes; careful rectal examination for evidence of metastatic nodules along the rectal shelf or in the pouch of Douglas; and careful palpation of the umbilicus, which is occasionally the site of disease that has extended down along the round ligament of the liver.

When any doubt as to operability exists the case should be explored, for it is not rare to find that cases that preoperatively appear to be of dubious operability are on exposure readily operable. On the other hand, in a recent case, which to all appearance beforehand was operable, it was only after a considerable amount of dissection that wide adherence to the pancreas was shown to make the growth inoperable.

The development of peritoneoscopy may aid in the recognition of inoperable cases that, in the past, have come to exploration. It is true that surgeons, impelled by a desire to overlook no chance for the patient, frequently explore cases in which they have little doubt of the inoperability of the lesion. In this group of cases where one finds peritoneal implants, liver metastases or ascites, peritoneoscopy has its greatest use. In the true borderline cases, however, we are inclined to believe that a small incision permitting digital exploration of the stomach, the gastrohepatic omentum and the liver is more informative than is peritoneoscopy, and certainly little if any more disabling. Parsons and Welch³ also emphasize the limitations of peritoneoscopy in this respect.

In 8 of our 68 cases we adopted some palliative operative procedure, such as jejunostomy, or anterior or posterior gastroenterostomy, with 1 fatality. This patient died a few days after operation, and no patient survived more than a few months. In 2 cases worthwhile relief from vomiting, lasting for a few weeks, has been afforded by posterior gastroenterostomy. Anyone who follows such cases to the end, however, must certainly question the wisdom of operative procedures of a palliative nature in cases in which the disease cannot be successfully extirpated. Only occasionally is the palliation afforded worth while. More often the end result is nothing more than a slight prolongation of the terminal stage of the disease. The point is made by Balfour⁴ that the surgeon must not extend palliation to inoperable patients at the price of a prohibitively high operative mortality. Such a mortality in this group would raise the general mortality for all gastric-cancer surgery, and would undoubtedly result in deterring operable patients from accepting surgery.

In this series there were 27 out of 63 cases (43 per cent, or 52 per cent of 52 malignant cases) in which resection was carried out. There were 4 postoperative deaths, a mortality of 15 per cent. Three of these were from peritonitis and 1 from bronchopneumonia.

Total gastrectomies were performed on 2 patients, both of whom were alive twenty months after operation. One of them has not been observed, but reports that he feels well and works every day. The second patient was recently reoperated on for bilateral Krukenberg ovarian tumors, and several small metastatic peritoneal implants were observed.

Sufficient time has not elapsed to make follow-up statistics in this series very valuable. In 1935, 1936 and 1937, however, 12 patients survived resection. Although 7 of these lived for two years or more, all but 1 of the group is now either dead or has a definite recurrence. In 1938 and 1939, 11 successful resections were done. All the patients are still alive, although 2, who have lived twenty months following operation, have recurrence.

SUMMARY AND CONCLUSIONS

Of 68 patients accepted for treatment with a preoperative diagnosis of gastric cancer, 5 proved on exploration to have either benign lesions or no demonstrable lesion. Of the remaining 63 cases, 11 (17 per cent) were not suitable even for exploration; 19 (30 per cent) were explored and found to be inoperable; 8 (13 per cent) were suitable for only palliative operations; 25 (40 per cent) received resection. Of the 27 resectable lesions, including 2 that were benign or borderline, 2 were so extensive as to require total gastrectomy. The mortality in the resected group was 15 per cent.

Study of this series emphasizes once again the oft-repeated and discouraging fact that temporization for weeks and months and late diagnosis in cases that should at once be regarded as possible cancer is almost the rule. Since there is no immediate prospect of any new therapeutic method by which the appalling mortality from this disease can be reduced, it becomes imperative to utilize to the full the knowledge we already have. The burden of responsibility rests on the medical profession, first in the education of the public to the necessity for seeking medical advice for vague epigastric distress, indigestion and dyspepsia in middle life; and secondly in the acquisition, ourselves, of the habit of demanding an exact diagnosis when such patients present themselves, by the energetic use of existing diagnostic facilities.

The results following resection in the operable cases are almost equally disheartening, but there is some encouragement in the knowledge that the last two or three decades have shown a slowly but gradually increasing salvage. For example, no longer ago than 1914, Friedenwald⁵ found only 9 resectable cases in a reported series of 1000; and in 1923, Cheever,⁶ in a review of 236 cases, found only 23 (10 per cent) resectable. In contrast with these figures, our resectability figure of 40 per cent, Walton's⁷ of 44 per cent and the high figures reported by all recent contributors convince us that

progress is being made. In earlier diagnosis, and perhaps in a more radical type of resection, lie the possibilities for continued improvement.

171 Bay State Road

REFERENCES

1. Harris, S.: The early symptomatology and the diagnosis of gastric cancer. *Am. J. Surg.* 31:225-236, 1936.
2. Allen, A. W.: Carcinoma of the stomach: with special reference to total gastrectomy. *Ann Surg.* 107:770-782, 1938.
3. Parsons, L., and Welch, C. E.: The curability of carcinoma of the stomach. *Surgery* 6:327-338, 1939.
4. Balfour, D. C.: Factors of significance in the prognosis of cancer of the stomach. *Ann. Surg.* 105:733-740, 1937.
5. Friedenwald, J.: A clinical study of one thousand cases of cancer of the stomach. *Am. J. M. Sc.* 148:660-680, 1914.
6. Cheever, D.: The operative curability of carcinoma of the stomach. *Ann. Surg.* 78:332-341, 1923.
7. Walton, J.: Carcinoma of the stomach. *Lancet* 1:1101-1107, 1936.

A NEW TYPE OF MEDICATION TO BE USED IN BRONCHIAL ASTHMA AND OTHER ALLERGIC CONDITIONS*

PRELIMINARY NOTE

ETHAN ALLAN BROWN, M.R.C.S. (LOND.), L.R.C.P. (ENG.)†

BOSTON

THIS paper presents a simple method for the symptomatic and prophylactic treatment of bronchial asthma, and especially for the attacks that occur during the night, some six or more hours after retiring. The advantages of medication directed against nocturnal dyspnea of this type are obvious, since the patient is spared an experience associated with acute physical and mental distress, more intense than those usually experienced during daytime activity. He is, however, also spared certain associated symptoms not always given the emphasis they deserve. Nocturnal asthma not only disturbs sleep, but when occurring some six hours after retiring may shorten the hours of rest so that the patient undergoes a slight but continuous nervous exhaustion. This in itself acts to the detriment of his daytime activity, and directly or indirectly, may make him prone to further asthma. When nocturnal asthma has occurred over a period of time, it may take on the characteristics of a conditioned reflex, in which case special treatment becomes more than usually difficult since the patient must, in addition, learn to unlearn a bad habit.

Certain physical factors are important. An attack of asthma tends to deform the chest, the deformity being noticeable for some time after the attack has ceased. Such deformity may be avoided by giving medication prophylactically. Attacks that take place during the day can be prevented,

but except for the medication to be described below, there is at present no simple method of treating, either symptomatically or prophylactically, bronchial asthma of the nocturnal type.

PREVIOUS METHODS OF TREATMENT

The range of present-day methods for the symptomatic treatment of bronchial asthma cover medications taken orally, subcutaneously, intravenously (in hospitalized patients) and by nebulizer. All are effective in controlling symptoms of moderate severity if taken when asthma occurs. Only two of these methods can be used prophylactically, and both fall short of perfection for the patient whose symptoms arise some hours after retiring.

Ephedrine taken by mouth is efficacious for only a few hours, the relief it brings rarely lasting the night. Doses sufficient to prolong the effect are associated with undesirable side actions, especially tremor, nervousness and insomnia. Sedatives in small amounts control these, but in large amounts may cause a "hang-over." Injection treatment by means of epinephrine in oil has its own special disadvantages. This type of injection, since the oil is difficult to handle and the syringe and needle must be perfectly dry, requires too elaborate a technic for the patient who lacks skill or intelligence. The reaction may be unpleasant and the swelling large and painful for some days. An accidental intravenous or back-seepage reaction causes nausea, vomiting, and headache of great intensity. Furthermore, the present cost of this type of treatment makes it prohibitive for the patient of

*The expenses for this work were partially defrayed by a grant from the Asthma Research Foundation, Boston.

†Physician-in-chief, Department of Allergy, New England Medical Center, instructor in medicine, Tufts College Medical School.

moderate means. It is also true that, although the pharmacologic effect of the epinephrine base may last from four to twenty-four hours, the maximum effect undeniably occurs during the first few hours following the injection, a time when the patient may in reality need it least.

The ideal solution of this problem was envisaged as a type of medication that could be taken at bedtime and by mouth. It should consist of time-tried drugs, and should become effective several hours after ingestion.

NEW METHOD OF TREATMENT

As a first step toward devising such a remedy, the various medications that might be used were investigated. Although several drugs of the ephedrine group were available, some were too new or too expensive. I have used ephedrine sulfate and sodium phenobarbital extensively for some years and have, in common with other allergists, found the combination valuable for the symptomatic treatment of bronchial asthma. For two years, theophylline sodium acetate has also been employed, with a synergistically enhanced effect. Capsules and tablets containing ephedrine, a sedative and one of the purines have been used for a number of accepted commercial preparations. Theophylline sodium acetate¹ has been shown in other fields of investigation to be superior to theophylline ethylenediamine, and this experience was repeated in the present series.

Capsules containing $\frac{1}{2}$ gr. of ephedrine sulfate, $\frac{1}{2}$ gr. of sodium phenobarbital and 3 gr. of theophylline sodium acetate were dispensed over a period of eighteen months to 189 patients encountered in private practice and in the Allergy Clinic of the Boston Dispensary. The medication was also utilized in other allergic complaints not included in this report, and in addition was sent to 171 physicians practicing allergy, for use on their private patients. Although their experiences paralleled those here described, the numbers and effects are not included in the present report. All the patients reported on in the present paper had bronchial asthma and were classified as follows: extrinsic, 80 cases; intrinsic, 50 cases; and mixed, 10 cases.

In every case in which the usual doses of ephedrine and phenobarbital were adequate, the capsule just described was equally or more effective. Psychologic factors are of course difficult to evaluate, especially for new medications. No objective method of measurement except the patients' statements could be found. The usual method of tabulation of results was not practical. No patient had an exact record of the number of attacks preceding treatment or, if possible to judge, of

their intensity. All patients were receiving treatment aimed at the fundamental causes of their difficulty. All except those who had side reactions, to be described below, agreed that the relief came on more quickly and was more complete than that given by other medications they had received. All refused to return to the previous medication while the new one was available. This was especially significant, since some of these patients used the capsules for symptomatic relief for more than eighteen months.

Of the total number of patients given the capsules, 13 complained of side reactions. These included tremor, palpitation and headaches due—as proved experimentally—to the ephedrine, small doses of which caused the difficulty. These patients were unable to continue with any ephedrine medication. Six of the patients who were given the capsules complained of nausea and indigestion. This was found to be due to the theophylline sodium acetate, and the patients were therefore given capsules without this component. Four patients complained of nausea, but because of the relief given by the three drugs combined, continued to take the capsules containing theophylline. No case of sensitivity to phenobarbital was encountered in the present series, and in no case was there a sedative "hang-over" due to the $\frac{1}{2}$ gr. of phenobarbital. Two patients complained that all gelatin capsules caused pyrosis.

ENTERIC-COATED MEDICATION

The dosage having been stabilized and its clinical effect proved, an enteric coating was manufactured. It was planned to have this dissolve in four or five hours. The coating contained cetyl alcohol, gum mastic, balsam of Tolu, gelatin, gum Arabic and sugar. Acetone, alcohol and water were used as solvents. The coating was applied in the usual way, a tablet of specific weight being placed in a rotary coating pan and the proper amount of coating material added. A mixture of warm and cold air was circulated through the mixture so that there was gradual and uniform evaporation of the solvent. The process was continued until the enteric coating was of the desired thickness. Samples were tested for disintegration in vitro with artificial gastric juice, and other tablets of the same coating but containing barium sulfate were used for testing in vivo. By experimentation on human subjects, roentgenologic evidence was obtained that the coating dissolved in three and a half to five hours.

Enteric-coated tablets were given to a total of 117 patients, of whom 61 also received the plain capsule, since asthma occurred either during the day or during the first four hours following retir-

ing. The remaining 56 patients had no asthma during the day but usually had symptoms arising four or more hours after retiring, and were given the enteric-coated capsules alone. It must be understood, however, that the classification was not always so clear as that implied; and those given both capsules and tablets had occasional nights when asthma occurred only during the first few hours following retiring or during the few hours before arising. The 61 patients, therefore, who received both capsules and tablets were those whose asthma might occur during either period of the night or both. When previous investigation showed their attacks to be irregular, they were controlled with both a capsule and a tablet given on retiring. Either medication alone protected only for its period of efficacy. The remaining 56 patients had asthma only during the hours preceding arising and therefore received only the enteric-coated tablets. So far as was practical, fecal examination was made as often as possible, and in all such cases none of the tablets were found to have passed through the intestinal tract undissolved.

Of the 117 patients, 8 complained of awaking six hours following medication. They were free of asthma, but unable to fall asleep again. This state was attributed to the theophylline, and either this drug was omitted or additional phenobarbital was given.

Patients who had asthma both during the day and at night showed the most striking improvement. The ability to sleep during the night lessened in almost all cases the number or intensity of daily attacks. This was especially true of the intrinsically asthmatic patients, a group recalcitrant to the usual treatment by capsules with theophylline sodium acetate. It must be mentioned that not all patients got relief at all times. For those attacks of great severity that were not helped in the past by ephedrine and phenobarbital alone, the capsules and tablets were also not effective except occasionally. If the patient suffered from moderate and mild symptoms, the new medication was definitely more effective.

Six patients not included in any of the above groups were treated while in status asthmaticus. They were given epinephrine in oil in doses varying from 1 to 2 cc., each cubic centimeter of the oil containing 2 mg. of epinephrine. The injections were given at 8 a.m. and 8 p.m. Because the work of Gaddum,² showing the enhancing effect of ephedrine on epinephrine, they were given the capsule described above at the same times. With the evening injection of epinephrine in oil they were given both the capsule and the enteric-coated tablet. Two of the 6 patients re-

quired additional medication during the night, but after the second day 4 were able to sleep all night. In previous attacks, and in attacks subsequently, in which epinephrine in oil was given alone, the effect did not last through the night. For these patients, the capsules and tablets given alone were not more than mildly effective.

CASE REPORTS

CASE 1. E. B., a 35-year-old man, had had "bronchial trouble" until the age of 7 and typically infective bronchial asthma from the age of 20. Attacks of status asthmaticus had occurred at intervals of 1 or 2 months, or less. The diagnosis was bronchial asthma and chronic asthmatic bronchitis. When not taking treatment, the patient had asthma associated with exertion and upper-respiratory infections. He also had symptoms following changes in barometric pressure. He quite commonly awoke in the early morning with an asthmatic attack, which usually required adrenalin. Capsules relieved him completely when taken for attacks during the day. The enteric-coated tablet and capsule taken at bedtime gave him a full night's sleep.

CASE 2. E. D., a 45-year-old man, had had chronic bronchitis in the winter of 1938-1939. In April, 1939, he had his first attack of asthma, which was very severe and is said to have lasted 17 days. The patient was hospitalized and had several attacks until July, but was free from them until December. He then had typical upper-respiratory infection and was beginning to wheeze again, and had asthma for 3 weeks following each cold and attack of bronchitis. Adrenalin gave only occasional relief. Ephedrine and Amytal relieved mild attacks. The patient had had morphine on various occasions. Skin tests showed a +++ reaction to feathers and a +++ reaction to dust. The capsules described above completely relieved the patient. A capsule and tablet at bedtime gave a full night's sleep. Asthma recurred during the night as soon as the medication was stopped.

CASE 3. E. D., a 39-year-old woman, first developed "asthma" 2 hours after birth. The attacks were perennial and continuous, with spasmodic exacerbations. There were no environmental or seasonal factors. The patient was worse when near the ocean and following nonspecific reactions such as excitement, distention, infection, barometric change, and the smell of fried food or gas. All the teeth and the turbinates had been removed. The patient weighs over two hundred pounds and is on a reduction diet. One capsule gives relief within twenty minutes. A capsule and a tablet give complete relief lasting all night.

CASE 4. J. S., a 45-year-old man, had bronchitis beginning in October or November each year from 1912 to date. In 1918 he had epidemic influenza. The first asthmatic attack occurred October 3, 1919. The patient was then entirely free from asthma until 1921, and then had spasmodic attacks at varying intervals coming on each fall but ceasing in the spring. He was first seen in August, 1939, when he was severely ill with status asthmaticus. He was given 1 cc. of epinephrine in oil at 8 a.m. and 8 p.m., and at the same time the capsule described above. In 2 days he was able to dispense with epinephrine, and all asthmatic attacks, although previously not controlled by ephedrine and Amytal, could be controlled by the uncoated capsule.

CASE 5. C. P., a 47-year-old man, had hay fever in 1919, and had treatment with ragweed extract every year except 1924 and 1928. The symptoms were seasonal until 1938. In January, 1939, the patient had his first attack of asthma. He had vaccine treatment with slight relief and had since had almost continuous asthma. He now obtains a full night's sleep on taking a capsule and a tablet, and only partial relief when taking either alone. Cessation of medication results in the immediate reappearance of symptoms.

CONCLUSIONS

Capsules containing $\frac{1}{2}$ gr. of ephedrine sulfate, $\frac{1}{2}$ gr. of sodium phenobarbital and 3 gr. of theophylline sodium acetate were used for the treatment of 189 allergic patients over a period of eighteen months. Of these, 140 had bronchial asthma. The mixture given in a standard gelatin capsule was found to be more effective than ephedrine and phenobarbital, given alone or combined with other purines.

A tablet with an enteric coating that did not dissolve for three and a half to five hours was used

for patients whose symptoms began in the early morning hours. For patients whose symptoms began at irregular intervals a capsule and tablet assured a full night's sleep. When used for patients more severely ill, they enhanced the effect of epinephrine in aqueous solution, or epinephrine in oil. The combined oral administration of a capsule and a tablet was effective in controlling symptoms for twelve to fourteen hours or more in patients who had had several attacks of asthma in a similar control period.

These same patients, spared the physiologic and psychologic upheaval of the unexpected attack of bronchial asthma and disturbed sleep, had less asthma during the day and for some subsequent nights when medication was omitted.

75 Bay State Road

REFERENCES

1. Riseman, J. E. F., and Brown, M. G.: The comparative value of prior derivatives in the treatment of angina pectoris. *J. A. M. A.* 105:25-258, 1937.
2. Gaddum, J. H.: Alkaloid ephedrine. *Brit. M. J.* 1:713-717, 1935.

DIVERTICULITIS*

JOHN F. ERDMANN, M.D.†

NEW YORK CITY

IN men, pain in the left lower quadrant, with nausea or vomiting, predicates diverticulitis of the sigmoid; in women, in whom this disease is of relative infrequency, such pain may mean any one of numerous diseases.

From 1919 to April 1, 1940, I operated on 90 patients for acute diverticulitis, of whom 69 were men and 21 were women. Carman¹ stated that there are two or three cases in men to every case in a woman. In my series, several patients had had multiple attacks. One had had two distinct perforations during a period of thirteen or more years, for each of which he was operated on. Several others had had two attacks and 1 three for which they had been operated on. The gangrenous perforations in each case were in demonstrably different areas.

In 1931 I operated on a fifty-one-year-old man for an acute diverticulitis with perforation. The operation was a suturing of the perforation. In 1933 he had another perforation fully 12 cm. above the previous site, and pus was found as high as the renal fossa. Suturing and drainage were successful. A third attack occurred on February 2, 1938,

when a fecalith 0.9 cm. in diameter was found free in a collection of pus. At that time I resected 15 cm. of the sigmoid after the method of Mikulicz, and fourteen days later opened the right lower quadrant of the abdomen, removing an exceptionally long and gangrenous appendix. Previous to the first operation the patient had had several attacks in the left lower quadrant that were treated with ice bags. Today he is in superb health, but I am always worried that he will have another attack.

I² called attention in 1918 to the possibilities of repeated attacks. My associate at that time, Dr. Thomas Russell, also found in one of his patients a second perforation, remote from the site of the first.

These succeeding gangrenous attacks, of necessity, call for a very guarded prognosis in a patient suffering a first attack. The number of patients I have seen and operated on for the acute condition has led me again to review the literature as to causation and to express my own views derived from clinical observations.

CAUSATION

Graser³ attributes the formation of diverticula to hernial protrusions, which, following the emerg-

*Presented at the annual meeting of the New Hampshire Medical Society, Manchester, May 15, 1940.

†Consulting (active) surgeon, New York Post-Graduate Hospital.

ing veins and taking a wandering course through the intestinal walls, finally reach the serosa. This conclusion was based on the study of 28 cases, from which he made more than a thousand sections.

Sudsuki¹ made a series of observations, contending that Graser's conclusions were fallacious.

Klebs⁶ noted that the protrusions occurred in close relation to points of exit and entry of the blood vessels in the intestine along the mesenteric attachment, and offered a series of arguments for these protrusions, chief among them being that the intestinal wall is weakest at the mesenteric attachment.

Klebs's argument is certainly fallacious, for in my series of patients, both those operated on and those in whom the protrusions were found to be inactive while I was operating for other causes, the most frequent site was that of the convex and lateral aspects of the colon, chiefly in the fat lobules or epiploons, and rarely in the mesenteric folds. Furthermore, the view of Klebs that mesenteric traction has a tendency to weaken the wall and is therefore a productive factor, appears to bear little weight.

Old age as a factor is disproved by 2 patients of Hartwell and Cecil,⁶ aged seven and ten, 1 of my own, a boy under seven, and a number of the patients under forty used as material for this article. Ransohoff⁷ reported the occurrence in 2 children and called the condition perforating sigmoiditis and perisigmoiditis.

Hartwell and Cecil, in summing up the etiology of this disease, after considering the various theories and arguments, were driven to the conclusion that "up to the present time no complete explanation of the primary cause of intestinal diverticula has been offered. The most that can be said is that, for some cause, a weakness exists in the intestinal coats, and that by reason of the weakness a pouching of the coats takes place when undue pressure arrives." I am inclined, from my clinical experiences and from roentgenographic observation, to the conclusion that diverticula are of congenital origin, although some may be acquired.

Reference to the literature and my own observations produce sufficient evidence that the entire alimentary tract from the esophagus to and through the rectum is liable to diverticula. During the last sixteen years I have operated on patients who had diverticula other than colonic. Among those were 6 or more duodenal, 1 gastric, several of the gall bladder, 3 of the cecum and ascending colon and several of the appendix. One of the appendicular operations was performed on a child under seven years of age. Many cases have also been observed, during various abdominal operations, of

diverticula scattered through the lesser as well as the greater curvature of the stomach.

In the patients with acute manifestations, some food or fecal content is often found in the pouch involved, leading one to believe that these foreign bodies act in the same productive manner as do the foreign bodies that are found in the appendix.

Diverticulosis is a condition in which many diverticula are found either by operation or by roentgen examination and today is a well-established disease, at least roentgenologically if not symptomatically or clinically. It requires but the onset of a pathologic process of one or more of the protrusions to become a definite clinical entity.

CLASSIFICATION

Although various classifications as to false and true, acquired and congenital diverticula have been in vogue, that of true diverticula, in which all coats of the intestine are present, and the false diverticula, in which one and usually two coats are absent, is the most popular and desirable for a working basis.

PATHOLOGY

The pathologic conditions found may be of as many varieties as there are types of appendicitis, from a simple catarrhal, better-called acute, type through those with exudative and occlusive changes to those with ulceration and gangrene with perforation. All these may or may not be accompanied by, or rather followed by, true abscess formation, and finally the acute processes may recur or never resolve and a malignant change may eventually arise.

These malignant changes are reported frequently enough to give some weight to the possibility of an implantation of a malignant nature on a former simple inflammatory growth. Nevertheless, even though in my series of patients with this disease I have found a malignant condition in 6 or 8, it seems certain that the condition is not a result of the disease but a coincidental state. It should be borne in mind, however, that location of the malignant implantation at the site of a prolonged irritation is always possible.

In many of these patients a low-grade infection exists, proceeding finally to a marked thickening and new growth, which at first resembles a malignant growth in its symptomatology as to partial or complete obstruction, and which roentgenographically may be so confusing at times as to demand exploration for a positive diagnosis by the microscope. One of the most frequent complications in the acute types is abscess formation with adhesions to a hollow viscus and perforation; the bladder is most frequently involved. This com-

plication occurred in several patients in my operative series, and in 1 patient not only was the bladder perforated but a contact portion of the sigmoid also, and two perforations of the ileum were present. A recent patient on the eleventh or twelfth day of his disease showed a 1-cm. perforation into the posterior wall of the bladder, passing an extremely foul urine mixed with fecal matter. On exposure by operation on the fourteenth day, two perforations in the sigmoid were found to be in contact with the bladder perforation.

On three or four occasions I have seen high perforations in the rectum which produced ischio-rectal abscesses, the origin of which in each was undoubtedly a gangrenous diverticulitis. Several patients had a history of sudden onset of pain, with the subsequent formation of this type of abscess.

That satisfactory spontaneous recovery occurs in cases of diverticulitis cannot be disputed, any more than it can be denied that patients with appendicitis, definitely evidenced by symptoms, make a nonoperative recovery.

Early in 1926 I removed 25 cm. of the sigmoid in a man fifty-four years of age, whom I had seen three years previously in an acute but subsiding attack, and who had been examined for mild attacks at various times during that period by his physician. His fourth attack, which required operation, was followed by the formation of a large mass in the left lower quadrant of the abdomen, encroaching on the hypogastric zone. On exposure not only was a marked amount of thickening and obstruction evident, but three large pockets of foul pus were evacuated.

During the last ten years I have removed various lengths of sigmoid for these conditions, one in a woman seventy-four years of age who also had an incarcerated femoral hernia.

SYMPTOMATOLOGY

It was formerly believed that an appendicular attack occurred in the left side as a result of the terminal portion of the appendix extending across to the left, or that there was a transposition of the appendix with infection. Although these cases—particularly the former type—do occur, it has been possible for years, in the great number of cases, to diagnose the condition definitely as diverticulitis.

The symptoms and signs are allied to the various types of appendicitis, such as the fulminating one, in which pain in the left lower quadrant rapidly develops, the pulse and temperature keeping pace with the invasion, together with abscess formation, distinct pain on pressure and finally mass or tumor formation. Eventually, if operation is

not performed, the following terminations may occur: death from peritonitis, resolution (occasional), perforation into a surrounding viscus (the bladder most frequently), ischio-rectal abscess, and in the event of nonresolution or nonoperative intervention, thickening of the intestinal wall and surrounding fat, so that obstruction of varying degree results. In the fulminating type, it may be that one must take refuge in the diagnosis and exploration of an acute condition of the abdomen. The diagnosis in women, as stated before, is difficult at times, owing to the many diseases that may arise in the tubes and ovaries.

In the subacute variety, a state of subsidence frequently occurs that enables the x-ray diagnostician to be of assistance. The very low-grade type with marked infiltration presents occasional evidence of obstruction in mild or incomplete form, with no evidence of blood or mucus as in carcinoma. With a proctoscope inserted to its full length one can eliminate carcinoma, at least in those patients in whom carcinoma starts in the mucosa, recognizing the fact that only a minimal number of cancers of the sigmoid or colon ever arise outside the mucosa. Nevertheless, I have never seen mucosa of the colon involved in a case of diverticulitis. The contrary holds true in malignant conditions. There is no more difficult procedure than that of seeing through a proctoscope the openings of any of these diverticula; yet one can conceive of the accidental exposure of a relatively small opening, or of the opening into a large diverticulum in which the mouth is also large.

DIAGNOSIS

In making a diagnosis of this condition, the general aspect and the age of the patients are to be considered. Most patients are short, stocky, well-nourished and overweight, usually in the fourth or fifth decade, and they give a history of some dietary indiscretion as is also frequently noted in taking the history of a patient with appendicitis. The youngest of my patients was under seven years of age and the oldest eighty-one, both males, whereas the majority were from forty to forty-eight.

The onset is characterized by abdominal pain that is more definitely located in the left lower quadrant than the pain in appendicitis. There is nausea or vomiting and a rapid rise in temperature and pulse, with concomitant tenderness on pressure in the left lower quadrant, varying in location from the iliac fossa, the usual site, to the mid-hypogastric zone. The blood examination gives the typical picture of an acute infection.

Rectal evidence as to the site of the involvement varies. If the lesion is high in the sigmoid little or no evidence is present, whereas if it is low

cated in the lower segment of the colon, ample signs can be detected, chiefly pain in the first few hours, followed by a palpable mass. Again, if the area involved is in the midsigmoid area, provided that sufficient mobility is present, the evidence may be obtained by combined rectal and suprapubic pressure.

The greatest difficulty in making an accurate diagnosis prevails in malignant cases with perforation, for owing to the perforation a temperature exists, and a tumor or mass is present, as may be the case in patients with infection without cancer. In the patient with carcinoma a careful history will often bring to light evidence of occasional pain, colic, constipation, loss of weight, blood (not found in diverticulitis) or mucus in the stool, tenesmus, frequency of desire to defecate or pain in the back, and blood examination may show a distinct secondary anemia. When it is possible to use x-rays without danger to the patient, these are frequently of great aid. The possibility of both diseases being present should be borne in mind.

GROSS PATHOLOGY

When the abdomen is opened, the intensity of the process varies. Noninflamed diverticula are seen protruding from any or all of the surfaces of the intestine. They are balloon-like elevations, resistant to the sense of touch, and may present evidence of containing foreign bodies.

The acutely inflamed type varies from a markedly injected diverticulum or epiploic appendix to one distinctly gangrenous. In the majority of patients on whom I have operated, one or more of the epiploic appendices in the vicinity were found to be involved by contiguity with the ultra-diseased one. These tabs of fat, epiploons or epiploic appendices, were either extremely hard and intensely injected or were in stages varying from hemorrhagic to gangrenous involvement. On section of the epiploic variety, near or at the base, a diverticulum is usually found. These bodies or pouches are round or oval, and range in size from that of a small seed to that of an olive, usually being about the size of a pea.

The resected colon, when opened, presents the appearance of a healthy mucous membrane thrown into folds, and here and there a crypt or long opening, into which probes of varying sizes may be introduced, some openings readily admitting a probe the size of a small pea. In various pouches round foreign bodies are present, which prove to be fecal concretions. The wall of the colon in chronic cases is thickened, the lumen diminished and the intestine quite often densely bound to adjacent structures.

McGrath⁸ has shown that most diverticula are of the false variety, and that the mucosa is pushed through the muscularis in the region of the penetration of vessels. In sharp contrast to this picture is that of the colon on section in malignant cases. The mucous membrane is destroyed. A deeply excavated area in the intestinal wall exists, with hardening of the tissue about it, and the lumen is irregularly compressed by the growth, if not completely annular. If the lumen is annular, the opening is diminished as the growth increases, a phenomenon similar to the closing of the diaphragm in a camera. The intestine contains sloughing, foul-smelling, purulent bloody material.

Among my cases of diverticulitis, 2 were in the cecum, 1 in the vicinity of the ileocecal valve and 1 at the beginning of the ascending colon.

I repeat that operation does not predicate a clean bill of health as regards occurrence or recurrence, since in 1 case over sixty-four diverticula were demonstrated in 12 cm. of a section of sigmoid removed for cancer; in all the other patients in whom careful search was made numbers of diverticula were found, not involved by inflammation.

Two of my cases, previously recorded,⁹ presenting definite attacks and coming to operation the second time, and the case cited above with the three attacks, each followed by operation and involving a sigmoid length of not over 15 cm., also constitute undeniable evidence of the possibility of repeated attacks. A guarded prognosis as to recurrence is naturally necessary. In my series there is a record of repeated invasion in 4 per cent of the cases.

Some of the earlier reports of long cures of cancer by resection must be taken less seriously at the present time and the cases considered as diverticulitis. I reported one such case, in which I operated on a woman in 1909 for an obstruction supposedly due to carcinoma. The entire pelvis was filled with a hard, nodular mass, the temperature was normal and a complete obstruction existed. A sigmoidostomy was done. In the course of two years all movements occurred by rectum except for a slight leakage through the contracted sigmoid anus. The patient was reported well many years later.

PROGNOSIS

In acute cases with early operation the prognosis is good, whereas in chronic cases with resection it is equal to that of all ordinary intestinal operations of approximately the same severity. Of 27 patients operated prior to 1919, 4 died, a mortality of 14 per cent; the mortality rate of the cases cited today is far lower.

TREATMENT

The acute condition of the abdomen presents but one solution in all patients in whom no cardiac or renal contraindication exists, namely, early operation. One should no more await resolution in an abdomen in the acute type of this disease than one should in an allied condition due to appendicitis, cholecystitis or salpingitis.

The habit into which some observers fall of waiting and using ice in acute abdominal cases may bring about occasional good results, but most frequently the outcome shows the effects of delay due to ignorance or poor observation. I have never seen the bad results that are said to follow immediate operation for acute salpingitis, acute appendicitis and ruptured tubal pregnancies, and I heartily condemn delay and applaud early surgical action.

In the chronic type of case no hurry is demanded, because positive obstruction rarely occurs. Partial obstruction is frequent. Here overzealousness should be subjugated to treatment, since it has been shown that the construction of an artificial anus proximal to the obstruction may work wonders in allowing absorption to take place in the thickened portion. As a result, the channel eventually approaches a normal condition. In other cases resection is necessary. Resection is frequently best done, and with the lowest mortality, by the Mikulicz procedure. End-to-end suture has a greater life hazard than the operation just mentioned, whereas side-to-side anastomosis is practiced only in certain cases.

Several types of acute cases in the early state should be considered. In cases in which the formation of a mass has not occurred, attempts to repair the perforation are indicated and meet with great success. Where abscess exists, liberal drainage and, when feasible, attempts at repair are indicated. In the event of partial obstruction, the establishment of an artificial anus proximal to the perforation and obstruction at times brings excellent results.

A fair proportion of these two varieties of cases may present a fistula for a few weeks or months after operation. It is invariably of small caliber and is easily taken care of and need cause no alarm, for healing is the rule. In several patients the fistulas have lasted for a few weeks,—one for four years,—and eventually all have healed. Between the establishment and the cure of the fistula, only an occasional visit to the surgeon, for attention to granulations, is necessary. Multiple fistulas require active intervention.

In 1936 an interesting case came under my care. It was impossible to repair a large gangrenous,

perforated diverticulum and drainage was established. During his time in the hospital the patient had two attacks of pneumonia and pleurisy with effusion. After discharge he had a single opening, which closed and reopened at intervals, and at the end of two years remained permanently closed. While on a cruise in the South Seas he had an attack of acute appendicitis and was operated on by a ship's surgeon. The boat headed for Honolulu, the first landing place possible, but the patient died as they were nearing port.

I now have under my care a man on whom I operated last spring. He has from 1 to 3 per cent sugar in his urine, and his stay in the hospital was very stormy. He has a well-established fistula with a tendency to repair and is able to control his sugar.

One interesting case was that of a man about sixty-nine years of age on whom I had done a perineal resection of the lower rectum for carcinoma. He was in the habit of attaching an enema tube to the tap in his bath and washing out his colon. One day the pressure became so great as to rupture the bowel. On opening the abdomen it was found that a diverticulum had been ruptured. The water had entered the peritoneal cavity, and a general peritonitis followed, with death.

In 1905 a physician from a neighboring state, rather short, obese and in his early forties, complained of pain in the lower left quadrant. This was followed by fever, an increase in pulse and mass formation. I opened the abdomen and drained an abscess, without doing any further exploration. Subsequent to recovery the patient developed a fistula, and after a few months' treatment his fellow-practitioners sent him to Rochester, Minnesota. There he saw the late William Mayo, who advised no interference, since it was an exceptionally small opening and did not hinder the patient in his professional duties.

In acute cases in which the diverticulum is situated between the plates of the peritoneum in the mesentery, it has been my custom for several years to split the peritoneum on both sides parallel to the vessels, in order that freer drainage may occur from the fat of the mesentery and hence that the possibility of retroperitoneal lymphangitis, the most vicious type of absorption, may be diminished.

The behavior of an artificial anus in a recent patient of forty-four, with a gauze and rubber-dam drain, was not so good as expected. The patient had chills with fever for days, so that by the seventeenth day a secondary abscess was drained. At about the seventh week a closure of the artificial anus was done, but the anus broke open on the ninth or tenth day afterward. Secondary sinuses formed. Although the patient's chest had been

repeatedly examined for tuberculosis, the observations had all been negative. A roentgenogram revealed an abscess cavity in the right apex fully 5 cm. in diameter and a dense infiltration of the entire left lung. There was no cough at any time, and very scanty sputum. An examination of the sputum showed that it contained innumerable tubercle bacilli. The patient has been sent west to a higher and drier zone. At neither of the abdominal operations was there any visible evidence of peritoneal tuberculosis. He recently reported that he was in excellent health and that the fistula was still present.

SUMMARY

Diverticulitis is usually a disease of the left lower quadrant, but may occur anywhere along the length of the colon and small intestine.

It occurs in males four times as often as in females; the greatest incidence is between forty and fifty years of age, but attacks in children have been reported. The patients are usually well developed, short, fat and overweight.

Diverticulosis rarely presents any symptoms sufficiently diagnostic to focus the physician's attention, but in a series of gastrointestinal roentgenograms this condition is often found. If diverticu-

losis is present and the patient gives a history of acute attacks of low abdominal pain, the former is likely to receive slight attention so far as the prevention of the latter is concerned. However, one can but suggest proper attention to the bowels in these patients, being careful not to make the patient so conscious of his anatomic or pathologic conditions as to become a mental invalid.

The presence of a diverticulum in the intestine merits no more attention than does the existence of the appendix or gall bladder, except that there may be many diverticula, whereas there is only one appendix and one gall bladder. Therefore, ordinarily the chance of acute diverticulitis is greater, but clinical evidence shows that diverticulitis is far rarer than disease of the gall bladder or appendix.

122 East 70th Street

REFERENCES

- 1 Carman R D The roentgenologic findings in three cases of diverticulitis of the large bowel *Ann Surg* 61 343 348 1915
- 2 Erdmann J F Acute diverticulitis of colon *New York M J* 109 969 972 1918
- 3 Grazer E Ueber multiple falsche Darmdivertikel in der Flexura sigmoidea *München med Wochenschr* 1 721 723 1899
- 4 Sudzuki K Ueber Divertikel am S romanum *Arch J klin Chir* 61 708 716 1900
- 5 Klebs E *Handbuch der pathologischen Anatomie* Vol I and II 528 pp Berlin August Hirschwald, 1869 Pp 271 273
- 6 Hartwell J A, and Cecil R L Intestinal diverticula a pathological and clinical study *Am J M Sc* 149 174 203, 1910
- 7 Ranshoff J Acute perforating sigmoiditis in children *Ann Surg* 58 218 225, 1913
- 8 McGrath, B F Intestinal diverticula their etiology and pathogenesis *Surg, Gynec & Obst* 15 429-444 1912
- 9 Erdmann J F Diverticulitis of colon *Am J Obst & Gynec* 11:609-616, 1926

RADIATION TREATMENT OF PLANTAR WARTS*

JOSEPH H. MARKS, M.D.,† AND CLIFFORD C. FRANSEEN, M.D.‡

BOSTON

THE incidence of plantar warts has appeared to increase in recent years, owing perhaps to the increasing popularity of sports and the frequent use of school and public shower baths and locker rooms by large numbers of people. They occur most frequently in persons of high-school and college age. Their commonest site is beneath the heads of the metatarsals, but they may appear on any part of the foot.

The symptoms of plantar warts range from slight discomfort on direct pressure to marked disability and even actual confinement to bed. The proper treatment has frequently been long delayed through failure of the physician or podiatrist to recognize the condition. The patient is not infrequently treated for a "painful callus" for months

and even years before the correct diagnosis is made; the pain has in many cases been relieved for longer or shorter periods of time by paring down the overlying callus, but permanent relief is not obtained until the wart is destroyed.

In any painful callus, careful search for a wart should be made. On weight-bearing surfaces warts do not project above the surrounding skin as on the hands, but are flat and are usually surrounded by callus formation. Small, reddish or brownish-black dots may be seen through the callus, or may be made evident by moistening the callus or paring away the less translucent superficial layers. These dots represent the capillary loops of the wart. Some of them may become broken, and small amounts of dried blood may thus be deposited in the skin.

The present treatment of plantar warts does not lie within the field of any one medical specialty. They are treated by general practitioners,

*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 21, 1940

†From the Palmer Memorial Hospital, Boston

‡Roentgenologist, Palmer Memorial Hospital

Associate surgeon, Palmer Memorial Hospital

dermatologists, surgeons, x-ray and radium therapists and podiatrists. The diversity of methods used does not attest the simplicity of their removal, but rather the unsettled status of treatment, and a single patient is frequently treated by members of various specialties and by various methods before success is attained.

Warts, especially crops of numerous small warts, may disappear spontaneously; on the other hand, large isolated ones may stubbornly resist treatment. Because of the tendency toward spontaneous disappearance many superstitions have arisen, and whatever may have been done immediately preceding their disappearance is credited with the cure. Cures have been obtained by numerous methods that, in many cases, must have affected the wart only slightly. For example, disappearance of warts has been reported following accidental or intentional rubbing or injury by various objects, and also following the local injection of various solutions into their bases. Caustics, including strong acids and alkalis, have been very popular, especially among podiatrists. Multiple treatments are usually required, and frequently the caustic produces considerable discomfort after each treatment. Treatment by autogenous or typhoid vaccines and other foreign proteins has also been credited with cures. Prolonged courses of small doses of magnesium sulfate by mouth have been advocated, especially in children.

The experience with plantar warts at the Palmer Memorial Hospital has been largely limited to radiation treatment, which was attractive because it was painless in application, usually gave little or no discomfort during the reaction, and appeared to give a high percentage of satisfactory results. During the last two years, however, a number of unfortunate results of the treatment of plantar warts with x-ray and radium have come to our attention, and we have therefore undertaken a review of the 175 cases treated in this hospital between January 1, 1930, and May 1, 1939. Follow-up examinations on 50 of these cases have been made within the present calendar year, each of the patients having been treated at least twelve months prior to the follow-up examination.

Of the 175 cases treated, the primary treatment was by radium in 158 cases. Of these, radium was applied only once in 115 cases, twice in 26 and three or more times in 8. In 9 cases the primary radium treatment failed and was followed by some other method of treatment. Twenty-nine of the radium-treated patients returned for examination, and it was found that 22 were cured, 16 after one treatment and 6 after two or more treatments. Of the 6 cases which had been treated two or

more times, 2 showed minor atrophic change of the skin and 1 showed marked atrophy at site of treatment. It is believed that the latter patient may develop a radiation ulcer at a future date. In 7 of the cases the treatment with radium did not result in cure. The subsequent course of these 7 cases was as follows: 1 was cured by electrodesiccation and 1 by excision; 1 had a persistently painful wart within an area of atrophy, and 4 later received x-ray therapy in this or other hospitals. This group of 4 will be discussed in more detail below. The number of failures in the follow-up group is probably disproportionately high because it has seemed easier to follow those patients in whom the result was poor. Many patients with satisfactory results could not be persuaded to return for examination.

Fifteen patients were treated primarily by x-ray. The fact that this treatment was not used before 1937 accounts, in part, for the small number in this group. All these patients returned for re-examination one year or more after treatment. Ten patients showed complete cure, with only showing slight atrophy of the skin at the site of treatment. One, with the wart on the great toe, had such marked atrophy that amputation of the toe became necessary when ulceration occurred after trauma. One patient showed a small remnant of the original wart but was symptom-free. Three others failed to obtain cure by x-ray and were later treated successfully by electrodesiccation.

We wish to call special attention to a group of 6 patients who had x-ray treatment here or elsewhere following failure of radium to cure. Of these, only 2 had satisfactory end-results. The remaining 4 patients make up an unfortunate group who had radiation ulcers necessitating hospitalization for surgical procedures to replace the damaged tissues. Three required excision of the area of ulceration followed by plastic repair. One required amputation of a toe. All had received two or more radium treatments followed by x-ray treatment and had been treated over periods of five, five, nine and eleven years respectively. The experiences of this group of patients served as the stimulus for the present study, and we strongly urge that repeated heavy doses of x-ray or radium should not be employed in the treatment of plantar warts. The histories of these patients suggest that a long interval of time between treatments increases rather than decreases the danger.

It is our opinion that many of the enthusiastic recommendations of radiation treatment of plantar warts that have appeared in the literature are based on a follow-up examination made too soon

After the conclusion of the treatment and before the late end results were known. Although relief of symptoms may occur, recurrence may appear later, and when large or repeated treatments have been given there is always danger of trouble from the late effects of the radiation.

We believe that plantar warts may quite properly be treated by single, rather large doses of either x ray or radium, but that such doses should not be repeated and that the area so treated should not exceed 10 cm in diameter. When using radium we have screened the wart closely and have used up to 16 millicurie hours of radon filtered through 0.3 mm of steel. The applicators have been applied to the surface of the foot after the callus overlying the wart has been pared away. When using x ray, single doses of from 1200 to 800 r have been given, depending on the site and size of the lesion. Experience has shown that larger doses are required when the wart is situated in the tougher tissues of the ball of the foot than when the involved area is in the relatively soft tissues beneath the longitudinal arch or on the toes. We customarily use radiation generated at 200 kv and filtered through 0.25 mm of copper and 2.0 mm of aluminum.

We have for several years been accustomed to treat multiple warts on the hands with repeated, small doses of x ray at intervals of about one week, and have had excellent results. Our usual practice for such cases in adults has been to give three treatments of about 300 r each, but in children doses as small as 100 r may suffice. If reasonable care is used to protect the uninvolved area, it is unnecessary to shield closely the individual lesions; some warts completely disappear after one treatment, and most of them show some decrease in size following the second. At the third session the field to be treated is usually small, and occasionally treatment need be applied to only a few remaining lesions. Recently we have applied this same method to plantar warts in cases in which many lesions were present over a relatively large area. Since careful individual shielding of the warts is not necessary in this procedure, the minute satellite warts are less apt to be missed. The

method has so far yielded excellent results but has been used in only a few cases.

If the first treatment by radium or x ray is unsuccessful, patients with plantar warts may apply for additional treatment elsewhere, and in this manner may receive multiple treatments with radiation, with disastrous results. It is therefore important to warn patients not to permit repetition of such treatment, and similarly it is important to ascertain whether previous radiation has been given before treating any new patient. If previous treatment has been given, the exact dosage and site of treatment must be ascertained. If accurate information cannot be obtained, further radiation should not be given.

During the last year the majority of plantar warts have been treated by electrodesiccation, and the results have been highly satisfactory. The absence of late aftereffects, and the great certainty of complete eradication if the treatment is carried out thoroughly under adequate local anesthesia compensate for the slight discomfort produced by this method. It is essential to desiccate thoroughly the soft, active base of the wart that lies deep beneath the callus if the treatment is to be successful. In all cases where radiation has failed, electrodesiccation has succeeded in eradicating the wart. We have recently adopted the policy, therefore, of treating all plantar warts by electrodesiccation if a single massive treatment of x ray or radium has been given and has failed.

SUMMARY

Follow up studies on plantar warts treated by radium and x ray between 1930 and 1939 emphasize the fact that radiation treatment for this condition should be repeated only with the greatest circumspection when the single, massive-dose method has been used, no matter how long the interval between treatments. Radium and x ray treatment of plantar warts is attractive because of its simplicity and relative painlessness, but if a single treatment fails to cure, radiation should be discontinued. Electrodesiccation, when properly carried out, has given excellent results.

195 Pilgrim Road

REPORT ON MEDICAL PROGRESS

WARTIME PREVENTIVE MEDICINE

CHARLES A. JANEWAY, M.D.*

BOSTON

FOR centuries the civilian population has suffered from the train of misfortunes following in the wake of war. In the present and recent European conflicts, however, war itself has involved the people as a whole. Great cities have become the front line of battle, their inhabitants, and particularly those who work in industry, the nation's most important soldiers. Thus civilian public-health service can no longer be separated from military medical service, and public health in its largest sense becomes an essential means of maintaining national morale.

A broadly conceived program in wartime preventive medicine should operate in at least three main fields—psychiatry, nutrition and epidemiology. Psychiatric study of the effect of incessant bombing on individual health and efficiency seems eminently sound. Nutritional research and the prevention of diseases such as pellagra have already achieved a place in our national health program. The application of the recently acquired knowledge of the structure and function of the vitamins may be tremendously important in preventing epidemics of mental, political and infectious disease under the strain of war.

The control of infectious disease has always been recognized as a public-health function, and many lessons in this field were learned during the last world war. Although the great epidemic diseases smolder in other parts of the globe, the United States has been free of any serious epidemics since the influenza pandemic of 1918. With most of the rest of the world at war,—regardless of whether we become involved or not,—great vigilance will be required to prevent the resurgence of epidemic diseases. In wartime, masses of people are moved into new environments under crowded, unsanitary conditions, and thus the ideal situation is created for the spread of infection. The inevitable sporadic cases occur, and with many susceptible persons in close contact, the infection is rapidly transmitted from patient to patient, the infective agent increases in virulence and an epidemic is soon under way.

*Instructor in medicine and in bacteriology and immunology, Harvard Medical School; associate in medicine, Peter Bent Brigham Hospital.

IMPORTANT WARTIME INFECTIOUS DISEASES

The control of infections depends on a knowledge of their specific etiology and of their mode of spread. The first is the foundation of prophylactic immunization, the second essential for more efficient mass-control measures. Before considering details, I shall attempt to outline the scope of the problem that might arise in wartime. With airplanes, disease may reach us from other continents within a fraction of its incubation period, and its ultimate distribution would depend on the presence of susceptible persons, proper environmental conditions, sufficient insect vectors and so forth. Since our climate varies from arctic in Alaska to tropical in Panama, few diseases might not conceivably be brought to our civilians or troops.

The following list is far from complete, but includes the main infections that health officers and physicians might have to deal with:

Enteric Diseases.

- Bacterial. Typhoid and paratyphoid fevers, dysentery, cholera.
- Toxic. Botulism, staphylococcal food poisoning.
- Protozoan. Amebiasis.

Respiratory Infections.

- Virus. Colds, influenza, measles, smallpox, mumps, psittacosis, epidemic encephalitis (?).
- Bacterial. Diphtheria, hemolytic streptococcus, meningococcal and pneumococcal infections, pertussis, tuberculosis.

Contact Infections.

- Spirochetal. Yaws, pinta.
- Metazoan. Schistosomiasis, hookworm disease.

Veneral Infections.

- Virus. Lymphopathia venerea.
- Bacterial. Gonorrhea, chancroid, granuloma inguinale (?).
- Spirochetal. Syphilis.

Insect-Borne Infections (often from animal reservoirs).

- Virus. Dengue, yellow fever, equine encephalitis, St. Louis and Japanese B encephalitis (?).
- Rickettsial. Rocky Mountain spotted fever, typhus.
- Bartonella infection (?).
- Bacterial. Plague, tularemia.
- Spirochetal. Relapsing fever.
- Protozoan. Chagas's disease, malaria, kala azar (?).
- Metazoan. Filariasis.

Animal-Borne Infections.

Virus. Lymphocytic choriomeningitis.

Bacterial. Tularemia, brucellosis, tuberculosis, Haverhill fever.

Spirochetal. Weil's disease, rat-bite fever.

Traumatic Infections.

Bacterial. Pyogenic infections, gas gangrene, tetanus.

Some of these infections would be curiosities, others such as influenza or malaria might be a greater menace than an enemy invasion. Many are susceptible to control by proper sanitation, but to obtain maximum protection, immunization of the individual should also be used wherever possible.

SANITATION

Enteric Diseases

Typhoid fever is a rare disease in most large cities, but sanitary engineering has not succeeded in controlling the milder attacks of bacillary dysentery and acute gastroenteritis. Many mild ambulatory cases of diarrhea have been proved to be bacillary dysentery or salmonella infections. Since these patients are not hospitalized, and often not even seen by a doctor, the detection of carriers becomes almost impossible. Under military regulations, rigid examination of food handlers and strict supervision of the preparation of food may keep these infections in check in cantonments.

Control of toxic enteritis is more difficult. Botulism can be eradicated by proper methods of canning, but staphylococcal food poisoning, which results from the rapid growth of staphylococci in milk, cream, eggs, pastries and meat in a warm place, is hard to control. Heat will not destroy this toxin.

Although there are an appreciable number of carriers of *Endamoeba histolytica* in the United States, amebic dysentery is relatively rare. In tropical regions it is endemic. Its prevention depends on common-sense sanitary regulations aimed at all enteric diseases—cleanliness of food handlers, fly control and the proscription of all raw food in endemic zones.

With widespread bombing of cities now prevalent, water and sewage systems would inevitably be disrupted, and if civilians were evacuated to the country, control of water supplies would be very difficult. The public would have to be instructed about boiling all water and cooking all food, but compulsory vaccination of the civilian population against enteric fever would be essential.

Contact and Venereal Infections

These infections constitute a definite threat to our troops operating in foreign zones, particularly

in the Caribbean area. Obviously, the only preventive measures are education of the personnel, and in venereal diseases, individual prophylaxis. The use of condoms and careful washing or the instillation of protein silver solution and the local application of calomel ointment immediately after intercourse have been recommended.¹

Insect and Animal-Borne Infections

Mosquitoes of the *Aedes* group have been shown to be the vectors of a number of mosquito-borne virus infections. This was first demonstrated by Walter Reed and his associates for yellow fever in the Spanish-American War, and subsequently by other workers for equine encephalitis^{2,3} and dengue.⁴ *Aedes aegypti*, the yellow-fever mosquito, is readily controlled because it can breed successfully only in stagnant water stored in artificial containers about human habitations. Weekly inspection of houses will eradicate the insects, as Gorgas proved in Havana and the Canal Zone. Such inspection should be required in the Gulf States at least, now that airplane travel brings yellow fever within easy reach of our shores. Recent epidemics of dengue prove that sufficient *A. aegypti* can breed here, and that the danger of a yellow-fever outbreak is a real one. The United States Public Health Service exercises strict control over travelers from yellow-fever zones, but this cannot be so efficient as eradication of the vectors.

Although yellow fever has gone from tropical cities, it is endemic in the jungles of South America and West Africa. The ultimate reservoirs of the disease are unknown, but several varieties of *Aedes* mosquitoes native to the jungle can transmit the disease to monkeys and man. Here mosquito control is impossible, and hence the successful development of a method of immunization is of tremendous importance.⁵

Dengue has occurred in epidemics in the South several times in recent years. It has been transmitted to monkeys, and the virus has been cultivated on the chorio-allantoic membrane of the chick embryo. No satisfactory methods of immunization have yet been developed.⁶

The control of malaria is still a vast problem in the tropics. In many areas a large percentage of the population is infected, and although their infections remain latent most of the time, they serve as reservoirs from which the disease is transmitted to newcomers, who may develop severe clinical infections. The anopheline mosquitoes are wild breeders, and thus mosquito control involves extensive drainage of swamps and oiling of ponds and stagnant pools. For an army in malarial country, individual chemical prophylaxis with daily

doses of quinine seems to be the only feasible method.⁷

A very serious threat to the economic life and health of this hemisphere has arisen from the importation of a new mosquito, *Anopheles gambiae*, into Brazil from West Africa. This mosquito is a vicious biter, breeds particularly around human habitations, is very susceptible to infection and has no natural enemies in South America. Consequently, without the introduction of new strains of parasites, epidemic malaria has broken out wherever this insect has made its appearance. Barber⁸ states: "There is no doubt that this invasion of *Gambiae* threatens the Americas with a catastrophe in comparison with which ordinary pestilence, conflagration, or even war are but small and temporary calamities. *Gambiae* literally enters into the veins of a country and remains to plague it for centuries." The Brazilian government and the Rockefeller Foundation are waging a hard fight against this menace in an attempt to localize and exterminate the mosquitoes.

One of the most fatal epidemic diseases, plague, is transmitted by fleas and lice. Plague has its reservoir in rats, among which epidemics break out when the proper combination of many susceptible rats and abundant fleas appears. As the rats die, the fleas leave their hosts and may attach themselves to humans; thus the bubonic form of plague results. If sufficient human cases occur under crowded conditions, cases of pneumonia develop, plague bacilli are passed from person to person by droplet infection and the pneumonic form of plague occurs, with a mortality of about 100 per cent. Plague-infected wild rodents are distributed over a wide area in the Far West, and plague-infected rats are present in Louisiana, although human cases are extremely rare.

Rats form the reservoir for two other serious infections, typhus and leptospirosis (Weil's disease or epidemic jaundice). Classic or European typhus is passed from man to man by human lice, but on this continent typhus is essentially murine. If lice from infected rats attach themselves to man, typhus results, and it may then be passed to other humans or back to rats, depending on the whims of the lice. In southern Georgia and Alabama, and to some extent throughout the South, typhus cases occur annually, and these areas remain foci from which epidemics might spread. Mexico has always had typhus, particularly in the neighborhood of Mexico City.

Weil's disease bears considerable resemblance to yellow fever clinically, with high fever, jaundice, oliguria and albuminuria. It is caused by two varieties of leptospira — *Leptospira icterohaemorrhagiae*,

carried by rats, and *L. canicola*, carried by dogs. Infected but apparently healthy animals carry the organisms in the kidneys, and large numbers are shed in the urine. The infection is contracted through ingestion or mere contact with infected excreta, particularly in sewers and contaminated water. This disease has been reported in various parts of the country, some cases having occurred in Boston.⁹ Obviously the control of all these infections involves the protection of men from rats, which may be quite difficult when there is widespread destruction of buildings, docks and warehouses from air raids.

In this country we have a number of similar diseases, some endemic in wild animals, transmitted by the bites of various blood-sucking insects, which might cause trouble to large bodies of men operating in the field. Bubonic plague, mentioned above, and tularemia are widespread among wild rodents. Relapsing fever has been found in ticks in the Southwest, and Rocky Mountain spotted fever, the wild analogue of typhus, is endemic in the Rockies and in the Middle Atlantic states. Military surgeons and physicians responsible for the health of evacuated civilians must be familiar with the diseases of their districts, and should enforce strict precautions against blood-sucking insects, particularly ticks. The latter are capable of transmitting the etiologic agents of Rocky Mountain spotted fever, tularemia, and Western equine encephalomyelitis to their offspring, and hence are a perpetual menace.

Respiratory Infections

Undoubtedly the most contagious and difficult to control of all human infections are those involving the respiratory tract. Anyone interested in the problems that this group of diseases raised during the last world war should read the late Dr. Zinsser's recent paper,¹⁰ which gives the morbidity among the enlisted men in this country during 1917 and 1918 as 473,279 cases of influenza, 38,846 cases of measles and 102,950 cases of mumps. If a disease like pandemic influenza strikes, it is hard to see how any practicable mass-control measures can halt its spread, but doubtless attention to a few simple rules may reduce its morbidity and mortality. Zinsser suggested that new recruits be mobilized in small groups near home, toughened gradually, and not assembled in large camps in new regions until they are in excellent physical condition. Beds in sleeping quarters should be separated by at least six feet, and any man with a respiratory infection should be kept in bed until his symptoms subside. In hospitals, ultra-violet screens to kill air-borne bacteria and viruses pre-

ing through them are on trial,¹¹ but there are many difficulties in their application to military barracks.

How effective prophylactic administration of sulfonamide drugs to patients with influenza may be in preventing bacterial complications remains to be seen. But since the viruses of colds, influenza and measles pave the way for bacterial infections and since their spread is almost impossible to control, the development of methods of active immunization against these viruses seems essential.

IMMUNIZATION

Anyone who uses immunizing agents for the prevention and treatment of disease should be familiar with a few general principles of immunology. Therefore, I shall discuss these before considering the individual preparations now available.

Immunization may be either active or passive. The latter involves the injection of antibodies produced by another person or animal, and thus the recipient plays a passive role. Such an immunity is short lived, but immediately effective. Foreign serum, like tetanus antitoxin, is eliminated rapidly and conveys protection for only about two weeks; human convalescent serum is more slowly eliminated, so that its antibodies may be detected for about six weeks after its injection.

Active immunization involves the injection of antigenic material into the patient, thus stimulating him to develop his own immunity. It is the same type of immunity that is produced by the infection itself, except that the agent has been rendered innocuous, so that immunity arises without the development of the clinical disease. Whenever possible it is the best method since it is more permanent and effective. One of the great drawbacks to the use of antisera is that it has been impossible to separate the antibodies passively transferred from the principal that evokes an active immunity against the foreign serum. Consequently occasional anaphylactic reactions occur in serum sensitive people, and serum sickness frequently arises about ten days after injection.

A great variety of therapeutic serums are available for the treatment of disease, but unless they are used to prevent infection they are outside the scope of this discussion. The development of an active immunity to most infections requires a considerable length of time, — two to six weeks, — so that active immunization cannot be used for prophylaxis after exposure. Two exceptions to this rule are rabies, which has a very long incubation period, and smallpox, which has an incubation period considerably greater than that of vaccinia.

In other diseases, such as tetanus, immediate protection must be given with immune serum, which may be supplemented by active immunization for lasting protection. However, this has been modified by the clinical application of a well known immunological phenomenon. Once an active immunity has been established, even though the titer of circulating antibodies may be very low, another small injection of the antigen will evoke a rapid rise in antibody titer, often to a higher level than that originally attained. This has been applied to the maintenance of established immunity against typhoid fever, tetanus and diphtheria.

Vaccine is the name given to an active immunizing agent against disease. It may be a suspension of killed micro organisms for a bacterial disease, a suspension of infected tissue for a virus disease or an inactivated toxin for one of the bacterial intoxications. In making bacterial vaccines the organisms must be fully virulent, they must be killed by methods that do not destroy their antigenic potency, and the finished product must be kept under suitable conditions. The problem of vaccine production against many virus diseases is far from solved. Viruses will grow only in living tissue, either in infected animals or in tissue cultures. The tissue cells with the accompanying virus are killed by some gentle method, and thus the completed vaccine is a suspension of dead tissue. Other vaccines, notably those for smallpox and yellow fever and the Hogeys rabies vaccine, contain living but attenuated virus, and hence unless preserved in the cold lose potency very rapidly. The proteins of the virus infected tissue may act as antigens, sensitizing the patient. This seldom causes much trouble except with rabies vaccine, the first few injections of which may produce severe local reactions. Rivers and Schwenker¹² thought that the disseminated encephalomyelitis that has occurred in a few cases was probably due to sensitization against nervous tissue. Bacterial toxins and toxoids are far from being pure preparations, but represent filtrates of old cultures, thus including the ingredients of the culture media and the products of bacterial autolysis.

Enteric Infections

Vaccination against typhoid fever has unquestionably proved its effectiveness. As a result of the work of Grinnell,¹³ Felix and Pitt¹⁴ and others, the quality of the vaccine has been improved by maintaining the virulence of the strain used for its production. In this particular region a vaccine containing typhoid and paratyphoid B bacilli is sufficient, but for the military services it should probably contain a member of each of the *Salmo-*

nella or paratyphoid (A, B and C) groups. Vaccine immunity is not absolute, but most cases in vaccinated persons have occurred in those not receiving the full course of injections, and in general, cases in the vaccinated seem to be somewhat milder.¹⁵⁻¹⁷ The immunity probably lasts two years or more, but revaccination should be repeated annually where there is real danger of exposure. Recent investigations have shown that within several years of the primary immunizing course of 0.5, 1.0 and 1.0 cc. at weekly intervals, a single injection of 0.1 cc. of vaccine intracutaneously will produce a marked and rapid increase in protective antibodies.¹⁸ This method has the advantage of causing much less local or general reaction, and should be done annually or more often if necessary. Oral immunization against typhoid fever, recommended by Besredka¹⁹ because he thought it produced local immunity in the intestine, has not received general approval, and its results are far too irregular to supplant parenteral vaccination.

Prophylactic immunization against dysentery is sorely needed, but in the past the attempt has always been defeated by the extreme toxicity of the killed organisms. Another difficulty is the multiplicity of antigenically unrelated organisms that may cause the disease. At present there is no satisfactory vaccine available.

Cholera vaccination is widely used in the Orient, where a single large injection of vaccine is given. If a series of weekly injections were given it might produce a far more effective immunity. The most reliable statistics suggest that it conveys some protection against the disease, but proof is lacking.²⁰

Respiratory Infections

Experience has shown that diphtheria can be virtually eliminated by prophylactic immunization. In time of war, and certainly in the army, this should be obligatory, at least for all Schick-positive persons. There is a choice of three immunizing agents: toxin-antitoxin, a mixture of a very small amount of active toxin with an adjusted amount of horse antitoxin; toxoid or formalin-inactivated toxin, which can be given in comparatively large doses; and alum-precipitated toxoid. Toxin-antitoxin has two drawbacks: it is less efficient, and it contains horse serum and may sensitize the recipient. Any toxoid preparation has one disadvantage: it is apt to produce painful local reactions in adults, owing to the large amount of bacterial protein present as an impurity. Obviously, when chemical purification of the toxin can be carried out on a commercial scale, these reactions should disappear. Various means of detecting those apt to develop severe reactions to

toxoid may be used. In the performance of Schick test, a reaction at the site of the cor may be taken as indicating hypersensitivity to proteins of the diphtheria bacillus and as a warning that toxoid will produce a reaction. (A preliminary injection of 0.1 cc. of a 1:100 dilution of toxoid may be given intracutaneously. A positive reaction within forty-eight hours should be taken as evidence of hypersensitiveness and caution for the use of toxin-antitoxin, a negative as indication for the use of toxoid. In the French army, despite these drawbacks, the enlisted personnel has been regularly injected with toxoid but little is said about reactions in any of the French literature. Therefore, one may say that every effort should be made to produce pure toxoid commercially. Meanwhile, toxoid should be used up to the age of ten, but over that age should be used only with the realization that a number of painful reactions are to be expected unless tests are done to detect possible reactions. For mass immunization of adults, toxin-antitoxin is probably best at present. Most studies indicate that, whereas toxin-antitoxin is about 85 per cent efficient in reversing a positive Schick test, toxoid or alum-precipitated toxoid will be about 95 per cent efficient under proper conditions.²² Toxin-antitoxin immunity is slowly developed, requiring several months. The time factor is important, and it has been shown that injections spaced at intervals of three weeks are far more effective than those at weekly intervals. Alum-precipitated toxoid is to be somewhat more irritating than plain toxoid because of the alum, but requires fewer injections. Thus two injections of 0.5 cc. of alum toxoid or two months apart seem to be highly effective. Toxin-antitoxin is given as three 1-cc. doses, or as three doses of 0.5, 1.0 and 1.0 cc., four weeks apart.²³

Once such an immunity has been established a small secondary stimulus will produce a marked and rapid rise in the titer of circulating antitoxin. In some persons a Schick test is sufficient to this. The French army gives such an *injection rappel* a year after primary immunization with triple vaccine (typhoid-paratyphoid A and B, diphtheria toxoid, tetanus toxoid) to place the immunity on a solid basis.²¹

Pneumonia immunization was given several trials during the last war, with some fairly convincing results. Although handicapped by the multiplicity of pneumococcal types, the role of viruses in the pathogenesis of respiratory infection and the frequency of secondary infections with other organisms, the use of a mixed vaccine seems to have materially reduced the morbidity and mor-

of pneumonia in the mines of South Africa.²⁴ He is experimenting with chemical fractions of types 1 and 2 pneumococci. He believes that it may be possible to pick out those who are most susceptible to pneumonia and concentrate on immunizing them more heavily. Although active immunization against pneumonia is impractical in the life, it may be a valuable measure in large army establishments where the disease is apt to become epidemic.

The hemolytic streptococcus, unfortunately, also has a multiplicity of types, and seems to make a poor immunizing agent when killed. Little is known of the incidence of different streptococcal strains in disease in this country, and hence the production of an effective vaccine is still impossible. Commercial streptococcal vaccines and serums are few at present, unless Thalheimer's convalescent serums are an exception.²⁶

Immunization against meningococcal infection is hardly feasible in ordinary life, because the disease is so rare. However, with crowding such as occurs in military camps, meningococcal meningitis often becomes epidemic. Under these circumstances, prophylactic immunization with the strains isolated from the first cases has a rational basis. The results of previous attempts at protection by active immunization have not been encouraging, but they were not carried out under ideal conditions.

Since *Haemophilus pertussis* has been proved to be the cause of whooping cough, the vaccination of infants, six months to one year of age, is indicated. Large and numerous injections are required, and the duration of immunity is unknown.

Influenza and measles constitute the greatest problems in the field of respiratory infections. They are caused by viruses and spread by droplet infection, and hence their prevention demands an efficient vaccine. With influenza, the attempts in this direction have been handicapped by the short duration of immunity, the antigenic differences between strains and the lack of epidemic conditions to test the vaccine to the test. A fortunate occurrence in the laboratories of the Rockefeller Institute deserves mention, because it offers a possible solution to the problem.²⁷ To prevent the spread of distemper, a vaccine, made from the ground organs of influenza-inoculated ferrets who had died of distemper, was injected into healthy ferrets. A month later these animals were inoculated with a strain of influenza virus and were found to be immune. Further study showed that they had become immune not only to distemper, but to all strains of influenza virus available. This phe-

nomenon deserves the intensive study that it is now receiving.

Measles, unfortunately, seems to be transmissible only to monkeys, in which it produces an atypical and mild disease. Thus the production of vaccine is hampered by the lack of suitable test animals. Rake and Shaffer²⁸ have reported passage of the virus on the chorio-allantoic membranes of chick embryos for several generations, thence back to monkeys, but confirmation of their work is lacking. Convalescent serum and placental extract have been used in passive immunization against this disease, and doubtless have a place in pediatric practice. Their use on a large scale in military practice, however, seems scarcely feasible.

Smallpox should be classed with the respiratory infections. Its prophylaxis by vaccination is well known and recognized as essential by all authorities. Under conditions of stress, revaccinations should be carried out on all persons who have not had a successful vaccination within three years. It is important to emphasize that a vaccination is never successful unless there is some sort of reaction at the site. An immune person should show a papule at the site on the second or third day (immune reaction); a partially immune person should develop an accelerated vesicular reaction; whereas a susceptible person should have a typical "take" by the seventh day. If nothing happens, the lot of vaccine should be discarded and fresh vaccine obtained. Failures usually occur because the vaccine has been allowed to stand in a warm place. Although chick-embryo and tissue-culture vaccines have many theoretical advantages over calf-lymph virus, they have not proved their effectiveness, and the latter should be used at present.

Yellow Fever

Yellow-fever research advanced by leaps and bounds when it was found that the disease could be transmitted to monkeys and later to embryo chicks and white mice. As a result of many passages through mice and chick embryos, a strain of virus has become relatively innocuous to human beings, although retaining its antigenic properties. This living virus in chick-embryo tissue is an effective immunizing agent when injected subcutaneously, but must be maintained in a frozen, dried state until just before use. Over a million people have been inoculated, including the crews of the airliners flying to South and Central America, and no accidents have occurred.²⁹ The protection conferred in this manner seems to be effective and would be of tremendous importance to any armed forces operating in the jungle regions of South America or Africa.

Typhus

Knowledge of the etiological role of *Rickettsia prowazeki* in typhus and its relation to animal and insect hosts has made possible various schemes of immunization. Many ingenious methods to produce a vaccine have been tried,—the infection of lice, which were ground and injected, and the use of the tissues of rats that had been infected following the lowering of their normal resistance by x-ray treatments,—but these have now given way to cultural methods. Cox²⁹ has been able to make satisfactory vaccine by securing a high yield of rickettsia from the yolk sac of the chick embryo. Another method, which may make commercial vaccine production feasible, is the inoculation of agar-slant tissue cultures with infected yolk sacs, as devised by Zinsser, Plotz and Enders.³⁰ The rickettsia so grown in tissue culture can be harvested in large numbers, formalinized and used for inoculation. Similar methods are also applicable to the related disease, Rocky Mountain spotted fever.

The methods for the production of virus and rickettsial vaccines are far more difficult than those for bacterial vaccines, and will always require far stricter supervision and attention to minute details.

Tetanus

The prevention of tetanus is very much the same as that of diphtheria, except that toxoid may be used at all ages with less risk of reaction. Tetanus was appallingly common in the early days of the last world war, until the prophylactic injection of antitoxin into the wounded became routine. The present war has witnessed another advance: soldiers are going into the field actively immunized against this disease. Since wound infections are apt to be prolonged, this should obviate the need for repeated injections of antitoxin at later operative manipulations to prevent the development of delayed tetanus.

When a wound is received in such an immunized person, a single dose of toxoid to restimulate the production of antitoxin is all that is necessary. Within a week or ten days, the titer of antitoxin in the blood should reach higher levels than those achieved immediately after passive immunization.³¹ In a nonimmunized person, prophylactic antitoxin should be given, but active immunization with toxoid should be started at the same time, so as to give lasting as well as immediate protection.³²

Chemical and Mechanical Methods

The Spanish Civil War was not a complete disaster, because traumatic surgery learned some val-

uable lessons. These are embodied in a small book by Trueta,³³ which every military or civil surgeon who handles compound fractures and contaminated wounds should read. His program of treatment involves: operation as soon as possible, complete débridement, and complete immobilization of the wounded extremity in a plaster cast applied directly over the wound. Suppuration occurred in most cases, but, with immobilization of the part there was little tendency for the infection to spread and gas gangrene became very rare. Fever seldom lasted more than four or five days, and except for the foul odor of the discharges draining from the end of the cast, the local infection did no harm. By this method pain was relieved, generalized infection cut down and healing progressed in most cases with surprising rapidity.

The question that now arises and is still unanswered is what role the sulfonamide drugs may play in preventing infection in these wounds. British soldiers in the front lines have been given sulfanilamide tablets in their emergency kits with instructions to take them as soon as they are wounded. In animals these drugs are highly effective prophylactically, but the conditions are not those of the battlefield. Much work must be done, for example, studying the relative merits of oral and local sulfonamide therapy in preventing infection; the effect of the different drugs on the healing process and the length of time sulfonamides should be administered. The sulfonamides by mouth should at least delay the onset of infection during the critical period of transport to the hospital, and the combination of débridement, plaster immobilization and local or oral sulfonamide may eradicate infection altogether. It is impossible to be dogmatic about these things until sufficient reports on the use of these methods under war conditions in Europe are available.

Gas gangrene will probably be controlled most effectively by prophylactic sulfonamide, extensive débridement and immobilization than it ever will be by active or passive immunization. The latter was abandoned by the Spanish surgeons because of the success of other methods. However, the question also remains an open question.

SUMMARY

Changes in the technic of warfare have multiplied the chances of epidemic outbreaks of disease, and threaten to make civilian and military practice essentially similar in wartime.

Mass-control methods are to be used wherever possible, but they must be supplemented by methods of individual prophylaxis.

Active immunization is feasible against the following diseases of actual or potential danger in

time of war: typhoid and paratyphoid fevers and cholera; diphtheria, pneumonia and smallpox; typhus; yellow fever; and tetanus. Influenza and malaria probably constitute our greatest menace, because of the lack of effective means of control.

The improvements in surgical technic with débridement and plaster immobilization, active immunization against tetanus, the use of the sulfonamide drugs and rapid transportation to good hospitals by airplane should greatly decrease the mortality and disfigurement of the wounded.

721 Huntington Avenue

REFERENCES

- 1 Hazen H H, Hiscok I V, Pelouze, P S, Snow W F, Zisser, H, and Everett R. H. The chemical and mechanical prevention of syphilis and gonorrhea. *J A M A* 115:1185 1940
- 2 Davis W A. A study of birds and mosquitoes as hosts for the virus of eastern equine encephalomyelitis. *Am J Hyg* 32:sect on C 45:59 1940
- 3 Keller R A. Mosquitoes as vectors of the virus of equine encephalomyelitis. *J Am Vet M A* 82:757 771 1933
- 4 Bancroft T L. On the etiology of dengue fever. *Australasian M Gaz* 25:17 1906
- 5 Bauer J H. Yellow fever. *Pub Health Rep* 55:367 371 1940
- 6 Simmons J S. Dengue fever. In *Virus and Rickettsial Diseases* 907 pp. Cambridge Harvard University Press 1940. Pp 349 364
- 7 Castellani A. Medical aspects of the Italo-Ethiopian War. *Mil Surgeon* 81:1 16 1937
- 8 Barber M A. The present status of *Anopheles gambiae* in Brazil. *Am J Trop Med* 20:249 267 1940
- 9 Meyer K F, Stewart Anderson B., and Edd C B. Epidemiology of leprosy. *Am J Pub Health* 29:347 353 1939
- 10 Zisser H. On the medical control of mobilization. *Mil Surgeon* 87:214 220 1940
- 11 Wells W F, Wells M W, and Mudd S. Infection of air bacteriologic and epidemiologic factors. *Am J Pub Health* 29:863 880 1939
- 12 Rivers T M, and Schwenker F F. Encephalomyelitis accompanied by myelin destruction experimentally produced in monkeys. *J Exper Med* 61:689 702, 1935
- 13 Grinnell F B. A study of the dissociation of the Rawlins strain of *Escherichia typhorum* with special reference to its use in the production of antityphoid vaccine. *J Exper Med* 56:907 918 1932
- 14 Felix A and Pitt R M. Virulence of *E typhorum* and resistance to O antibody. *J Path & Bact* 38:409 470 1934
- 15 Topley W W C and Wilson G S. *The Principles of Bacteriology and Immunology* 1661 pp. Baltimore: William Wood & Co 1936 P 124
- 16 Sohier R and Paraise J. Les infections typho-paratyphoides des sujets vaccinés. *Rev d'immunol* 5:535 556 1939
- 17 Malinin B. Typhoid fever occurring in immunized persons. *J A M A* 115:33 36 1940
- 18 Siler J F and Dunham G C. Duration of immunity conferred by typhoid vaccine: results of re-vaccination by intracutaneous injection of typhoid vaccine of Laboratory Staff Army Medical School. *Am J Pub Health* 29:95 103 1939
- 19 Besredka A. *Les immunités locales* 224 pp. Paris: Masson et Cie 1937
- 20 Topley and Wilson's p 1124
- 21 Ramon G. Lanatosine tétanique et la prophylaxie du tétanos chez l'homme et chez les animaux domestiques. *Presse méd* 47:887 880 1939
- 22 Zinsser H, Enders J F, and Fothergill L D. *Immunity Principles and application in medicine and public health* 801 pp. New York: Macmillan Co 1939. P 527
- 23 Subcommittee on Diphtheria of the Committee on Evaluation of Administrative Practices. American Public Health Association. Recommended diphtheria immunization procedures. *Am J Pub Health Supp* 30:47 1940
- 24 Lister S and Ordman D. Epidemiology of pneumonia on the Witwatersrand Goldfields and prevention of pneumonia and other allied acute respiratory diseases in native labourers in South Africa by means of vaccine. *Publ South African Inst M Research* 7:1 81 1935
- 25 Felton L D. Immunization against pneumonia. *Am J Pub Health* 30:361 368 1940
- 26 Moore E and Thalmer W. Immunological properties of scarlatina convalescent serum. *Am J Dis Child* 58:1039 1046 1939
- 27 Horsfall F L Jr and Lennette E H. The synergism of human influenza and canine distemper viruses in ferrets. *J Exper Med* 72:247 260 1940
- 28 Rake G and Shaffer M F. Studies on measles. I. The use of the chorio-allantois of developing chicken embryo. *J Immunol* 38:177 200 1940
- 29 Cox H R. Use of yolk sac of developing chick embryo as medium for growing Rickettsiae of Rocky Mountain spotted fever and typhus groups. *Pub Health Rep* 53:2241 2247 1938
- 30 Zinsser H, Plotz H, and Enders J F. Mass production of vaccine against typhus fever of the European type. *Science* 91:51 1940
- 31 Jones F G and Moss J M. Studies on tetanus toxin: the response of human subjects to an injection of tetanus toxin or tetanus alum precipitated toxin one year after immunization. *J Immunol* 33:183 190 1937
- 32 Ramon G. Combined (active-passive) prophylaxis and treatment of diphtheria or tetanus. *J A M A* 114:2366-2368 19-0
- 33 Trueta J. *Treatment of War Wounds and Fractures With special reference to the closed method as used in the war in Spain* 146 pp. New York and London: Paul B. Hoeber & Sons 1940

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 26471

PRESENTATION OF CASE

A forty-two-year-old Jewish housewife entered the hospital complaining of crampy abdominal pain.

Two months before admission the patient began to suffer from intermittent, crampy pain in the right lower quadrant of the abdomen, which lasted for three or four minutes, occurred approximately twelve times a day and sometimes radiated to the left lower quadrant. She also noticed slight bleeding and pain on intercourse, especially near the time of her periods. For years the catamenia had been irregular, but on an average occurred every three or four weeks, lasted four days and required three pads. There had been slight intermenstrual bleeding for an unstated period. The last period had occurred one month before admission, followed by a slight vaginal discharge that was white, but not blood stained or of unusual odor. In addition the patient had suffered from constipation for three months, anorexia for two months and had lost 8 pounds in the month prior to entry.

The patient's father had died of diabetes at sixty, and her mother had died of "stomach trouble" at fifty-five years of age. Her three children, the youngest aged thirteen, were alive and well. The patient had had the usual childhood diseases, and for two years before entry a cough that was sometimes productive of white sputum. She had suffered from bleeding hemorrhoids for the previous two years.

Physical examination showed a well-developed and well-nourished woman in no apparent distress. Examination of the heart and lungs was negative; the blood pressure was 120 systolic, 70 diastolic. In the right lower quadrant of the abdomen there was a hard, movable, tender mass that was estimated to be between 10 and 15 cm. in diameter. Examination and culture of the urine were negative.

On the second hospital day a pelvic examination done under ether revealed a lacerated cervix and perineum, with some exposure of the endocervix. A large, fixed, irregular, sausage-shaped mass was palpable in the right lower quadrant. The uterus was movable and in fair position. In addition a

cystic mass the size of an orange was palpable on the left side. A laparotomy was then performed.

DIFFERENTIAL DIAGNOSIS

DR. LANGDON PARSONS: Obviously one's attention is chiefly focused on the pelvis as the source of this patient's difficulties. The pelvic symptoms were largely those of irregular and postcoital bleeding, together with dysmenorrhea and dyspareunia. Let us first consider the uterus. Immediate postcoital bleeding is always a danger sign pointing toward carcinoma of the cervix. On pelvic examination, however, exposure of the endocervix was the only finding. Moreover, carcinoma of the cervix is uncommon in Jewish women. It must be assumed that the bleeding was coming from higher up in the uterine canal, either from primary disease in the fundus or from secondary irritation associated with lesions in the adnexa. The presence of a fixed, tender mass tends to rule out a functional type of uterine bleeding. Despite the fact that the mass is spoken of as "fixed," the uterus is reported to have been movable. It would be unusual to have a carcinoma of the cervix or fundus of the uterus with such a mass as that described and with a freely movable uterus. A spread of cancer from this source to either the parametrium or the adnexa would result in a "fixed" pelvis. The description of the mass as sausage-shaped makes unlikely a diagnosis of a pedunculated fibroid with twist and inflammatory change secondary to circulatory damage.

One can go through all the possibilities of tumor of the ovary. If one presupposes a twist and subsequent inflammatory change to account for the degree of fixation, the diagnosis of an inflammatory ovarian cyst or tumor is an excellent explanation of many of the symptoms. The mass, however, is said to be large, irregular, sausage-shaped and fixed. The entire picture, with the anorexia and loss of weight, suggests cancer. A carcinoma of the ovary becomes fixed only after invasion of its serosal surface by disease. This results in a fixation of the pelvis floor, particularly of the uterus; however, the latter is said to have been movable. I have never seen a twisted carcinomatous cyst of the ovary.

The description, of course, most adequately fits disease of the fallopian tube, either infection or cancer. It would be unusual to have pelvic inflammation to the point of tubo-ovarian abscess or hydrosalpinx without having more fixation of the uterus. Carcinoma of the tube is rare; only 350 cases are reported in the literature. The physical findings in this patient, however, are consistent with it. The colicky pain could be caused by

spasmodic contraction of the tube as it attempts to extrude its contents, since the fimbriated end of the tube closes late in the disease. Tubal cancer is frequently bilateral, and although it may arise in an adenoma, an earlier history of salpingitis is very common. I do not believe the diagnosis of carcinoma of the tube will hold. Since the history and physical examination are not typical of an old ectopic pregnancy, the combination is enough to rule this out as a probability. So much for the pelvis.

Is this process primary in the genitourinary tract, or may it not be localized in the gastrointestinal tract, with secondary irritation of the pelvic organs? There is enough about this case to suggest that the lesion is not in the uterus or adnexa. In the first place, the recurrent colicky pain, the constipation over a period of three months, the weight loss, the anorexia and the bleeding from the rectum all point toward the large bowel. It is true that the bleeding is said to have come from hemorrhoids. A perforating carcinoma of the sigmoid looms large in the list of probabilities. The mass is said to have been both tender and fixed. The fact that it is fixed on the right side of the pelvis does not rule out sigmoidal cancer, for we have all seen such occurrences. On the other hand, the lesion may be purely inflammatory, with the mass arising from a perforation of an inflamed diverticulum. Cancer, however, is more likely. Is the disease primary in the left colon, with metastasis to the ovary, such as Krukenberg tumor? There does not seem to be enough fixation of the pelvic floor to explain retrograde lymphatic extension of this sort. Carcinoma of the cecum is a possibility, the only evidence of which is the presence of a fixed tender mass in the right lower quadrant. No mention of an accompanying anemia is made. There is no evidence for an appendiceal abscess.

I believe that the process is due to carcinoma, with possible perforation, arising in the gastrointestinal tract, with the location its only reference to the pelvic organs. Diverticulitis is a possibility.

DR. JOE V. MEIGS: This patient's history may have been overcondensed in the abstract, and perhaps it does not present the picture fairly. She did not look sick, but she had a huge mass in the right lower quadrant that could be seen. On pelvic examination an additional mass was found on the left side that was definitely cystic. She had been complaining of discomfort in the right lower quadrant for six weeks, but admitted very little in the way of gastrointestinal symptoms. The temperature was 102°F. when she came in. Knowing that she had a cyst of the left ovary, I thought

that she probably had a tumor or cyst of the right ovary, which was twisted. She was operated on without further study.

The left ovarian cyst was easily removed. While we were attempting to find the right ovary to identify the nature of the mass on the right side, an abscess was broken into that proved to communicate with the lumen of the cecum. The process appeared to be inflammatory, and it was assumed that we were dealing with an appendiceal abscess. Although there was nothing to suggest cancer a biopsy specimen was taken from the wall of the cecum. A tube was sutured into the bowel, and a drain placed in the abscess cavity. Much to our surprise the specimen was reported as an adenocarcinoma. Subsequently an ileotransverse colostomy was performed. The patient has done well, and it is planned at a later date to resect the cecum.

PREOPERATIVE DIAGNOSES

Ovarian cyst, left.

Ovarian tumor, with twisted pedicle?

Appendiceal abscess?

DR. PARSONS'S DIAGNOSIS

Carcinoma of the intestinal tract.

ANATOMICAL DIAGNOSIS

Adenocarcinoma of the cecum.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: It seems to me that Dr. Parsons's diagnosis proves that the abstract was not so inadequate. This is another example of the difficulties that occasionally confront the surgeon in distinguishing between inflammatory and neoplastic tissue. In a case recently discussed by Dr. Arthur W. Allen* the gross appearance suggested neoplasm, but eventually it was proved to be an appendiceal abscess. In this case everything suggested an inflammatory mass, but biopsy proved the underlying lesion to be carcinoma.

*Case records of the Massachusetts General Hospital. Case 26431. *New Eng. J. Med.* 220:676-678, 1919.

CASE 26472

PRESENTATION OF CASE

First Admission. A nineteen-year-old boy was admitted to the hospital complaining of dyspnea of seven weeks' and nausea of three weeks' duration.

At the age of twelve the patient had had what were said to be "growing pains." Following a "cold" he became very nervous, and his mother noticed that he could never sit still. He was ex-

aminated in the Out Patient Department, where diagnoses of residual chorea and rheumatic heart disease with mitral stenosis and regurgitation were made. He was given aspirin and put to bed for two weeks, and since that time had been followed in the Out Patient Department. Five years before entry the ankles became swollen, slightly painful, tender and stiff, and soon the knees, elbows and wrists were similarly affected. This illness lasted for two months, during which he was given aspirin, with the application of oil of wintergreen to the joints. Five months later a basal diastolic murmur was first heard. The patient was working as a grocery clerk at this time and remained symptom-free with restricted activity, but it was noticed that the heart was increasing gradually in size. Two months before entry he was required to lift heavy boxes, and this strain marked the onset of exhaustion at night, a dull precordial ache and the development of dyspnea, which finally prevented him from lying flat in bed. His physician kept him in bed and prescribed digitalis for the next five weeks; then the onset of nausea and vomiting precluded its use. During the two weeks prior to admission the patient had experienced a constant dull ache in the calf muscles of the left leg. He had lost 10 pounds in the previous six months.

The past and family histories were noncontributory.

Physical examination showed the patient to be slightly dyspneic. The neck veins were distended. A heaving cardiac impulse was situated at the anterior axillary line in the sixth intercostal space. The rhythm was completely irregular, with an apical rate of 138 and a radial pulse of 80. The area of dullness in the third interspace was increased. There was a coarse, short apical thrill that was practically synchronous with the apex thrust. A low systolic murmur and a marked mid-diastolic rumble could be heard at the apex. The aortic second sound was faint, and the pulmonic second exaggerated. At the base a faint, short systolic murmur was heard in the aortic area and a long, loud, high-pitched diastolic murmur along the left border, loudest in the third and fourth interspaces and associated with a diastolic thrill. The blood pressure was 140 systolic, 80 diastolic. The liver was palpable two fingerbreadths below the right costal margin.

The temperature was normal, and the respirations 22.

Examination of the urine was negative. The blood showed a red-cell count of 5,600,000 with a hemoglobin of 90 per cent, and a white-cell count of 14,600. The sedimentation rate was 0.55 mm. per minute, and the hematocrit reading 50 per

cent. The blood Hinton test and blood cul were negative. Electrocardiographic record showed auricular fibrillation, with a ventricular rate of 60 and slight right-axis deviation.

X-ray examination of the chest showed heart to be markedly enlarged to the left, with largement of the left auricle. The pulmonary vessels were widened, and there was a small amount of fluid in the left costophrenic angle.

The patient improved with digitalis and intravenous Salyrgan, and was discharged two weeks after admission with instructions to remain in bed for one month and continue the digitalis.

Final Admission (one year later). For the previous year the patient had been followed in the Out Patient Department, where examination indicated that the general condition had improved slightly. He had lived a greatly restricted existence, spending much of the time in bed under constant medical supervision. About one month before admission he developed a sudden palpitation and the heart beat heavily and rapidly. This was accompanied by nausea and vomiting, and within an hour developed a pain in the right lower axilla that was made worse by breathing. He went to bed immediately and for the next week intermittently coughed up blood. During this month in bed he suffered from general malaise, anorexia and some migratory joint pains. He lost 15 pounds weight.

On examination the patient had obviously lost ground. The skin and scleras were icteric, and the neck and fundal veins pulsating. The whole chest pulsated, and the cardiac apex was situated at the midaxillary line in the sixth interspace. The right border was percussed 4.5 cm. to the right in the fourth interspace, and cardiac dullness extended 6 cm. to the left of the midsternal line in the second interspace. The rhythm was completely irregular, with a rate of 150; pulsus alternans was present. In addition to the auscultatory findings noted at the first admission, there was a continuous, soft, blowing murmur at the apex and a high-pitched musical systolic murmur in the tricuspid area. The blood pressure was 160 systolic, 60 diastolic. Rales were heard over the second left anterior interspace at the base of the heart, and a dry, rasping friction rub was present over the entire right-lower-lung field. The tender pulsating liver was palpated 3 cm. below the right costal margin, but there was no peripheral edema.

The temperature was 100°F., and the respirations 25.

The urine showed a +++ test for albumin. The red-cell count was 5,500,000 with a hemoglobin of 85 per cent, and the white-cell count 13,000.

The serum van den Bergh was 2.5 mg. per 100 cc. A blood culture was negative. Electrocardiographic recordings showed auricular fibrillation, with marked right-axis deviation and sagging ST intervals in Leads 2 and 3.

X-ray study of the chest showed a fairly well-defined area of markedly increased density in the right-lower-lung field, in addition to the findings on the previous examinations.

The patient improved, but on the third day the temperature began to rise and he complained of upper substernal distress on deep inspiration, nausea and vomiting. One week after admission the friction rub had practically disappeared and the excursion of the right chest was diminished. There were, however, dullness, decreased tactile fremitus and breath sounds, and increased vocal fremitus over the right base and axilla. In the evening of the seventh hospital day the patient suddenly became apprehensive, dyspneic and extremely cyanotic and cried out in alarm. The blood pressure and radial pulse could not be obtained; the apex rate was 136; and the temperature had risen to 105°F. He improved in an oxygen tent but died rather suddenly four hours later.

DIFFERENTIAL DIAGNOSIS

DR. C. EDWARD LEACH: The first paragraph of the history in this case gives an etiologic diagnosis that I see no reason to dispute. However, there are some interesting points in the patient's later course that are worth discussing, and it would be interesting to try to determine what the status was at the time of death.

He was first seen in the Out Patient Department shortly after what was supposed to be the first attack of rheumatic fever, but at that time mitral stenosis was already present. To account for such an advanced lesion, I should expect that rheumatic infection was present at an earlier date than the history indicates. He apparently had laboratory evidence of active disease for only two weeks, for he was allowed out of bed after that time. Another episode of rheumatic infection occurred about two years later, subsiding in two months, but five months later a basal diastolic murmur was heard for the first time. Then, without further clinical flare-up, progressive increase in the size of the heart was noted during the three years before the hospital admission. These new signs might have resulted from the second clinical attack of rheumatic fever. If so, why were they not apparent with, or shortly after, the acute illness? I think the long latent period greatly favors subclinical rheumatic infection after the acute attack as the cause of the further heart damage.

The heart failure that made it necessary for the patient to enter the hospital was apparently precipitated by unusual physical strain, but it is also not unlikely that auricular fibrillation was an additional factor. We cannot tell when he began to fibrillate, but the chances are that it was a recent occurrence, because the badly damaged heart would not have been able to stand the strain of fibrillation without failing very soon. Digitalis was started on the outside but was stopped because of nausea. The rate was thus uncontrolled on entry but was soon controlled—the electrocardiographic rate was 60—with additional digitalis. It is well to mention here that nausea per se is not necessarily a sign of too much digitalis. In heart failure, nausea is a frequent concomitant of congestion of the abdominal viscera, and in gauging digitalis dosage one must consider other evidences of toxicity, such as unusual slowing of the cardiac rate and ectopic beats.

On physical examination, heart failure was indicated by dyspnea, engorgement of the neck veins and hepatic enlargement. The lack of peripheral edema can be explained by the buffer effect of the liver, which, at this stage of the disease, was able to take care of the systemic congestion. The heaving cardiac impulse, especially, if it were diffuse, indicated muscular hypertrophy of the right ventricle. The presence of aortic stenosis is suggested by the combination of an aortic systolic murmur and a faint aortic second sound. However, against such a diagnosis we have a pulse pressure of 60, absence of a thrill and the fact that the murmur was said to be faint. Other signs indicated the presence of mitral stenosis and regurgitation and aortic regurgitation, but the diastolic blood pressure of 80 suggests that there was not a great deal of aortic regurgitation, in spite of the fact that the diastolic murmur was marked.

One would like to be able to decide whether or not the patient had active rheumatic infection or other complicating factors at this hospital entry. The elevations of the sedimentation rate and the white-cell count were not referable to the heart failure alone and must be explained.¹ Phlebitis was suggested by the history of pain in the legs, but was not supported by further evidence. We have no evidence from the history or examination of other common causes of leukocytosis, such as urinary infection, pulmonary infarction and pneumonia. Thus, with no other likely explanation for the laboratory abnormalities and on the basis of our experience in similar cases, it is reasonable to assume that this boy had active rheumatic infection at the time of this admission. The electrocardiogram and the x-ray findings merely serve

to confirm the clinical diagnosis. I do not know why he had fluid only in the left pleural cavity. More commonly fluid accumulates first on the right side in heart failure. Perhaps the cardiac enlargement in this case contributed by interfering with venous return in the left chest.

The response to treatment in the hospital was good so far as the heart failure was concerned, and the patient was able to go home in two weeks. However, in spite of constant care and continued digitalization, it was necessary for him to lead a very restricted life, spending much of his time in bed for the next year. Evidently the damage already suffered by the heart had left almost no cardiac reserve.

Then, one month before the second hospital admission and about a year after the first, more trouble occurred. The history at that time of sudden cardiorespiratory symptoms, with rapidly increasing pleural pain followed by bloody sputum, is typical of pulmonary infarction. I suppose we should consider rheumatic pulmonary lesions, as well as pneumonias of other types, as a possible explanation of these symptoms. Paroxysmal tachycardia with resulting pulmonary edema might produce a similar picture. None of these alternatives seem very likely. Rheumatic lesions in the lungs usually accompany severe rheumatic fever rather than a quiescent infection and do not dominate the clinical picture to this extent. The rapidity of onset, the prominence of cardiac symptoms at the start and the type of sputum are all against lobar pneumonia or bronchopneumonia. If it were severe enough to give the other symptoms, pulmonary edema secondary to paroxysmal tachycardia could be ruled out by the duration alone. Pulmonary infarction is the only thing that I can think of that fits.

When the patient entered the hospital for the second time, the physical status had changed considerably from that previously recorded. There was increased congestion of both the neck veins and liver. There was more enlargement of the heart. The entire chest was pulsating. The heart rate of 150, in spite of the fact that he had been taking digitalis continually, was evidence of strain from a factor other than the heart itself. I should not consider the observation of pulsus alternans to be of any significance; it would be difficult, if not impossible, to determine in the presence of auricular fibrillation. The continuous, soft, blowing murmur heard at the apex was a new sign and might be explained either by changes in the mitral ring with the increase in heart size or by transmission of murmurs from the aortic area. A lower diastolic blood pressure indicated that the aortic re-

gurgitation had increased since the previous entry. In addition, the marked pulsations of neck vein and liver, together with a systolic murmur in the tricuspid area, indicated the likelihood of tricuspid regurgitation as a further diagnosis. The chest signs were consistent with consolidation from any cause.

The slight temperature elevation of 100°F. and the white-cell count of 13,000 were both in keeping with pulmonary infarction. The abnormal urine might best be explained by chronic passive congestion of the kidneys, since we have no reason to suspect other types of renal involvement. The serum van den Bergh was elevated, perhaps due to the congestion of the liver. It is well to mention, however, that peculiar hepatic lesions are found in fatal cases of fulminating rheumatic fever.² I do not think we need consider them here.

The electrocardiogram is interesting because it showed a marked degree of right-axis deviation. Berliner and Master³ reported that marked right-axis deviation was not found with mitral disease alone, but indicated an associated tricuspid lesion. Pulmonary infarction might also increase the right-axis deviation, but usually not to this extent. The electrocardiogram, taken with the physical findings, is strong evidence in favor of the diagnosis of tricuspid regurgitation.

The patient's course after entry was rather brief. On the third day he had further pulmonary distress that might have been due to another pulmonary infarct. The upper substernal distress was not a typical pain for pulmonary infarction. I suppose we must consider pericarditis, but I can find no confirmation of that in the record. The diminished excursion of the right chest suggested the probability of increasing fluid in the pleural cavity from the infarcts and heart failure. The terminal episode likewise appeared to be pulmonary, dyspnea and cyanosis being associated with a rise in temperature. Since the apex rate was noted at 136 without further comment, it seems safe to assume that no change in cardiac rhythm accounted for the sudden death.

To sum up, we have a boy of nineteen with a history of at least two definite attacks of rheumatic fever. Evidence such as progressive increase in heart size, progressive valvular disease and diminishing cardiac reserve indicated the probability of continuous, low-grade rheumatic activity over a period of years. At the time of final entry to the hospital he had mild joint pains. Although the heart failure cleared up well the first time, cardiac reserve was so poor that he remained a cardiac invalid for the year preceding death. I should ex-

t to find evidence of active rheumatic infection at autopsy in one who had run such a course, I believe it must have been found in this case. The question of organic versus functional tricuspid disease also arises. The same things that suggest continuous rheumatic activity favor the occurrence of organic disease of the tricuspid valve. On the other hand, the physical signs were mainly those of tricuspid regurgitation, and there had been considerable increase in heart size between the two hospital admissions. Furthermore, the pulmonary infarcts, with resulting strain chiefly on the right side of the heart, would tend to cause tricuspid regurgitation. It is likely, therefore, that we shall find slight rheumatic involvement of the tricuspid valve; dilatation of the tricuspid ring, however, will probably account for most of the incompetency.

Two likely sources for the pulmonary emboli occur to me. In rheumatic patients with fibrillation, emboli come oftenest from auricular thrombi. However, it is much more likely for the emboli to break off soon after fibrillation begins, rather than a year later. In all types of hospital cases the leg veins are common sources for emboli. Theoretically the patient showed no clear-cut signs of phlebitis that would not rule it out, since we know that pulmonary embolism frequently occurs some time before there are any signs of phlebitis. We have no positive evidence either way, and I am afraid that at I must leave this question open.

My diagnoses are rheumatic heart disease, both chronic and acute, auricular fibrillation, mitral stenosis and regurgitation, aortic regurgitation, and tricuspid regurgitation — chiefly dilatation of the ring but with some rheumatic lesions as well. Autopsy should also reveal considerable enlargement of the heart and chronic passive congestion of the viscera, probably with cardiac cirrhosis of the liver. There will be multiple pulmonary infarcts, the emboli having come either from an auricular thrombus or from the veins of the legs.

DR. BENJAMIN CASTLEMAN: Have you anything to add, Dr. Bland?

DR. EDWARD F. BLAND: I have nothing to add to what Dr. Leach has said, but I might mention for gain a point occasionally brought out in the conferences when we try to explain jaundice in patients with heart failure. I am not sure whether Dr. Leach mentioned it or not. Jaundice in this situation is often secondary to pulmonary infarcts. I should agree that the patient died of active rheumatic disease.

DR. HOWARD B. SPRAGUE: My impression is that jaundice in cardiac failure is most commonly due to pulmonary infarction.

CLINICAL DIAGNOSES

Rheumatic heart disease with mitral stenosis and aortic regurgitation.
Auricular fibrillation.
Acute rheumatic pancarditis.
Rheumatic pleuritis, right.
Pulmonary embolism.

DR. LEACH'S DIAGNOSES

Rheumatic heart disease, chronic and acute, with cardiac hypertrophy.
Mitral stenosis and regurgitation; aortic regurgitation; tricuspid regurgitation, chiefly functional.
Auricular fibrillation.
Cardiac failure.
Chronic passive congestion of the viscera, with cardiac hepatic cirrhosis.
Multiple pulmonary infarcts.

ANATOMICAL DIAGNOSES

Rheumatic fever, acute.
Endocarditis, acute and chronic with stenosis: mitral, aortic and tricuspid.
Pericarditis, chronic fibrous, rheumatic.
Cardiac hypertrophy.
Pulmonary infarcts.
Renal infarcts.
Cerebral degeneration (cortical).
Passive congestion of lungs, liver, stomach and duodenum.
Pleuritis, chronic fibrous, bilateral; acute fibrinous, right lower.
Hydrothorax, right.
Ascites.
Cholesterosis.
Jaundice.
Petechial hemorrhages of the pleura.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: This patient showed the usual anatomic signs of heart failure. There were 400 or 500 cc. of fluid in the abdomen and 200 or 330 cc. in each pleural cavity. The liver was enlarged and somewhat firm, and histologically showed not merely central necrosis but some fibrosis, so that one might call this a very early cardiac cirrhosis. Certainly there was not enough cirrhosis in itself to produce jaundice, which was probably due to the combination of liver impairment and extensive pulmonary lesions. There was a very large infarct at the costophrenic angle, and a more recent hemorrhagic area proximal to the infarct, which on gross examination appeared to be a rheumatic pneumonia. Histologically the latter area

showed extensive hemorrhagic extravasation into the alveolar sacs, and similar but smaller foci were found in the other lobes as well. These corresponded to what we have been calling rheumatic pneumonia, which seems to be merely a focal hemorrhagic process in the lungs. There were also petechial hemorrhages on the pleura, which is further evidence of active rheumatic infection. Examination of the heart valves revealed still more evidence of active rheumatic infection. There was disease of the mitral, aortic and tricuspid valves, each of which showed a row of fresh rheumatic nodules along their lines of closure. The histological picture of these lesions was characteristic of acute rheumatic infection, the palisading of the monocytes that has been described by Leary,⁴ for example. The heart was hypertrophied and weighed 550 gm. This hypertrophy was more marked on the right side, where the ventricular wall measured 8 mm. in thickness. The mitral valve presented a buttonhole aperture, measuring 2 by 1 cm. The aortic valve showed interadherence of the cusps. In one place the interadherence measured 1 cm. and appeared pulled down into the ventricular cavity, which I am sure produced some regurgitation as well as stenosis. Further evidence of regurgitation was the presence of a fibrous band of endocardial thickening in the ventricle, just below the valve, a finding that is sometimes spoken of as a fourth cusp. The tricuspid valve was not stenotic. It measured 13 cm. in circumference, but the chordae were slightly thickened. The leaflets themselves appeared fairly thin and pliable, despite the recent endocarditis. There were several small thrombi in the left auricu-

lar appendix. We could not find any in the right, but possibly there had been some that had broken off. The popliteal veins were free from thrombi, so that I am not able to explain fully the source of the pulmonary infarcts. There were also infarcts in the kidneys, which may account for the albumin in the urine; these were, I should think, fairly old.

DR. BLAND: It might be of some passing interest to mention that before the patient died, in the illness prior to the last, he had one or two tiny petechial hemorrhages on the conjunctiva that caused a little discussion; the point was brought out that they are not so significant of bacterial endocarditis as perhaps might be thought. They are not infrequently seen in other debilitating diseases, and we occasionally see them in a patient very ill with rheumatic fever.

DR. CASTLEMAN: I forgot to mention that the heart muscles in a number of sections showed no Aschoff's bodies and that the pericardial fat was completely obliterated by old adhesions. The older rheumatic infection must have involved the pericardium. There was no evidence of anything fresh in the pericardium.

Some diffuse cortical degeneration was also apparent on microscopic examination of the brain. No emboli or focal areas of softening were found.

REFERENCES

1. Kinsey, D., and White, P. D.: Fever in congestive heart failure. *Arch. Int. Med.* 65:163-170, 1940.
2. Bland, E. F., and Jones, T. D.: Fatal rheumatic fever. *Arch. Int. Med.* 61:161-171, 1938.
3. Berliner, K., and Master, A. M.: Mitral stenosis: correlation of electrocardiographic and pathologic observations. *Arch. Int. Med.* 61:37-57, 1938.
4. Leary, T.: Early lesions of rheumatic endocarditis. *Arch. Path.* 13:1-22, 1932.

The New England Journal of Medicine

Formerly the
Boston Medical and Surgical Journal
Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE
ON PUBLICATIONS

Official Organ of

THE MASSACHUSETTS MEDICAL SOCIETY
THE NEW HAMPSHIRE MEDICAL SOCIETY
THE VERMONT STATE MEDICAL SOCIETY

EDITORIAL BOARD

Joseph Garland M.D.	John P. Sutherland M.D.
William B. Breed M.D.	Stephen Rushmore M.D.
George R. Minot M.D.	Henry R. Viete M.D.
Frank H. Lahey M.D.	Robert M. Green M.D.
Sheldon Warren M.D.	Charles C. Lund M.D.
George L. Tobey, Jr., M.D.	John F. Fulton M.D.
C. Guy Lane M.D.	A. Warren Stearns M.D.
William A. Rogers M.D.	

ASSOCIATE EDITORS

Thomas H. Lanman M.D.	Donald Munro M.D.
Henry Jackson, Jr. M.D.	
Walter P. Bowers M.D.	EDITOR EMERITUS
Robert N. Nye M.D.	MANAGING EDITOR
Clara D. Davy	ASSISTANT EDITOR

SUBSCRIPTION TERMS: \$6.00 per year in advance postage paid for the United States; Canada \$7.04 per year; \$8.52 per year for all foreign countries belonging to the Postal Union.

MATERIAL for early publication should be received not later than noon on Saturday.

This Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway Boston, Massachusetts.

'GREEN LIGHTS TO HEALTH'

In recent years the importance of the physician-patient relation has been subject to much discussion. There is no gainsaying the fact that both the lay and professional press abound with comment and suggestions as to the need of perfecting this important influence that involves not only the health of the individual but also the physical fitness of the entire nation. The county and state medical societies, as well as national associations and federal agencies, stress more and more the urgent need of close co-operation and understanding between the public and the medical profession.

How can this be accomplished? First, there is the personal relation between physician and patient, which has existed in private practice for centuries. Due to the complexity of modern life we now find that another aspect has developed. It has evolved as a result of the vastness of public-

health control and the dependence of the profession on the public in supporting and co-operating in public health measures. For the two to work in harmony and to accomplish what is necessary, the public must have a clear understanding of the aims and workings of the medical profession and the public health agencies, and it is with this in mind that efforts are made to enlighten the public regarding medical matters.

If it is a fact that "the public thirsts for medical knowledge," this demand should be satisfied in an appropriate and forthright manner by the members of state medical societies. There is, however, a difference of opinion among physicians as to the expediency of the education of the public in health matters. Is the physician going to accept this responsibility, or is he going to continue to ignore the layman's plea and allow it to be answered by cultists, charlatans and mendacious commercial radio propaganda? The answer seems obvious, particularly in view of the fact that these evil influences have a great hold on the population.

Evidently the members of the Committee on Public Health and the Subcommittee on Public Education, who have been sponsoring the "Green Lights to Health" broadcasts for the past eleven years, feel justified after due consultation and study in using the radio as a medium of reaching the public. The radio stations of Boston are said to reach a potential audience of three million listeners, and it is reasonable to assume that they should be used as one means of approach in the field of health education.

It must be recognized that owing to the marked complexity of medical science it is hopeless to think that the layman can absorb any great amount of knowledge concerning health or pathologic states. If medical information can be presented in a manner to attract attention to the broad principles of medicine rather than to specific diseased states, the layman will be benefited. Such honest and accurate information and friendly approach to the people will give them confidence in the medical profession and a desire to retaliate by co-operating with physicians and the public health agencies.

WALTER CHANNING DAY

WITHIN the duration of any of Man's institutions there are raised up, either by fact or fiction, certain persons who by their precepts, teachings and initiative may be designated the founders of these institutions. Rarely do the disciples of such men obtain greater stature. Indeed, these disciples are often prone to accept without due appreciation the true and lasting values of the institutions so founded. In these days of uncertainty, when all is in flux, it appeared most appropriate to reaffirm in the present and re-establish with the past the value of one of the oldest and largest maternity centers of this country, the Boston Lying-in Hospital. This was done for the first time on October 24, 1940, on the one hundred and eighth birthday of the hospital, when its medical alumni returned to exchange professional knowledge and renew friendships.

The day was designated "Walter Channing Day," in commemoration of Dr. Channing, co-founder of the hospital and the first professor of mid-wifery and medical jurisprudence at the Harvard Medical School, or the Massachusetts Medical College as it was then called. He was also the first dean of the school, a position he held until 1847, when he was succeeded by Oliver Wendell Holmes. Dr. Channing contributed much to the medical knowledge of his time. He is perhaps best remembered as the earliest advocate of anesthesia in labor. Under his guidance the first woman in an American maternity hospital to receive an anesthetic, Catherine Fisher, was given ether in the Boston Lying-in Hospital on September 16, 1847, eleven months after its first public demonstration at the Massachusetts General Hospital. It is of more than passing interest that even today ether is probably the safest general anesthetic for use in childbirth.

During these years the institution has grown from a small house on the outskirts of the city to a modern hospital situated within a stone's throw of the Harvard Medical School. In the earlier years 27 women were confined annually. During the past year the various departments of the hospital cared for over 4000 patients, the

equivalent of every fourth baby born in Boston being delivered under the auspices of this institution. During the hospital's existence it has graduated 500 house officers, trained 6000 nurses and instructed 7000 medical students.

The physicians who have come under the influence of this institution have made many noteworthy contributions to clinical medicine. Many of these demonstrate a continuity of medical knowledge that mortises the past with the present. The following are typical examples of work that has been or is being accomplished.

The first use of ether to relieve the pain of childbirth was followed in recent years by the first study of the use of modern methods of analgesia in labor.

Hemorrhagic disease of the newborn was first described in this hospital. A recent voluntary assistant was one of the first to point out the value of vitamin K in the treatment of the hemorrhagic tendency of the newborn.

The first water-heated bassinet in America was devised in this hospital. The present institution has one of the most complete premature nurseries in the country, and it has been demonstrated that the death rate of premature infants can be decreased by two thirds with the use of such modern equipment.

It was the second hospital in America to develop and use an antiseptic technic at childbirth, which markedly decreased the incidence of puerperal sepsis. In recent years, the clinic has demonstrated the value of the combined use of sulfanilamide and immunotransfusion in the treatment of this dread disease.

This maternity hospital was the first to establish a clinic for pregnant cardiac patients, and during the last five years the clinic has conducted a most complete scientific study of the changes in the circulation during pregnancy.

Within recent years the hospital has made valuable contributions to the knowledge of both normal and abnormal embryology.

It appears that the medical heirs of Dr. Walter Channing have succeeded in keeping his name to the fore as being the founder of one of the

great institutions in America dedicated to increasing and distributing knowledge of what constitutes the best in maternal care

MEDICAL EPONYM

EWING'S SARCOMA

Dr James Ewing, oncologist and professor of pathology at Cornell University Medical College, New York City, discussed "Diffuse Endothelioma of Bone" before the New York Pathological Society and published his paper in the *Proceedings of the New York Pathological Society* (21-17-24, 1921)

For some years I have been encountering in material curetted from bone tumors a structure which differed markedly from that of osteogenic sarcoma was not identical with any known form of myeloma and which had to be designated by the vague term round cell sarcoma of unknown origin and nature. They occurred in subjects from fourteen to nineteen years of age. The tumors grew rather slowly requiring some months to attract attention, but they were accompanied by attacks of pain and disability. The radiographs give characteristic features on which a diagnosis may be based with considerable certainty. A large portion or the whole of the shaft is involved but the ends are generally spared, contrary to the rule with osteogenic sarcoma. The shaft is slightly widened but the main alteration is a gradual diffuse fading of the bone structure. Bone production has been entirely absent. Some of the bones appeared honeycombed. Perforation of the shaft and sharp limitation of the process are wanting. The central excavation with widened bony capsule, as seen in benign giant cell tumors is missing. The probable endothelial nature of the tumor was suggested by the form of the cells, and especially by the appearance in broad sheets of polyhedral cells without intervening stroma. The possible relation of the endothelial tumor to plasma cell or other forms of multiple myeloma deserves consideration.

R W B

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

RAYMOND S. TITUS, M.D., *Secretary*
330 Dartmouth Street
Boston

TOXEMIA ASSOCIATED WITH DIABETES AND RESULTING IN INTRAUTERINE DEATH OF THE FETUS

Mrs. W., a thirty-year-old primipara with diabetes of four years' duration, was first seen on March 25, 1935, when she was approximately twenty-four weeks pregnant.

The family history was noncontributory. The past history was irrelevant except for the diabetes, which had developed after a thyroid operation and had been controlled with insulin. Catamenia began at thirteen, were regular with a twenty-eight-day cycle and lasted five to six days without discomfort. The last period began on September 24, 1934, making the expected date of confinement June 30.

At the time of the first visit the patient had gained 10 pounds in the previous month, the weight being 167 pounds. The blood pressure was 120 systolic, 66 diastolic. The fundus was 21 cm., above the symphysis, and the fetal heart was audible. There was no edema.

On April 8 the insulin dosage was increased from 26 units to 36 units a day. The blood sugar was 90 mg per 100 cc. The weight was 170 pounds. The fetal heart was heard. The blood pressure was 120 systolic, 70 diastolic.

On April 25 the patient was receiving the same insulin dosage. The weight was 179 pounds. The blood pressure was 130 systolic, 80 diastolic. The fundus was 26 cm. above the symphysis, and the fetal heart was audible. The patient complained of edema of the legs.

On May 2 the legs were less swollen. The patient was taking 32 units of insulin a day. The weight was 178 pounds, and the blood pressure 124 systolic, 80 diastolic.

On May 10 the weight was 177 pounds. The blood pressure was 128 systolic, 90 diastolic.

On May 14 the weight was 179 pounds. The blood pressure was 142 systolic, 88 diastolic. There was a great deal of edema, and the urine contained a very large trace of albumin. The patient was sent to the hospital, on May 16 the blood pressure was about 145 systolic, and there was a trace of albumin in the urine. The fetal heart was audible. By May 19, when the patient was thirty weeks pregnant, she had lost 4 pounds, and the blood pressure was down to 120 systolic. The fetal heart sounds could no longer be obtained. On May 23 the blood pressure was 120 systolic. The urine still contained a trace of albumin, but the patient's condition was satisfactory and the uterus was shrinking.

On May 31 the weight was 169 pounds. The blood pressure was 120 systolic, 80 diastolic. The blood sugar was 60 mg per 100 cc. The patient was discharged from the hospital and returned to her home.

On June 13 the weight was 172 pounds, and the blood pressure 114 systolic, 68 diastolic. The blood sugar was 70 mg per 100 cc. Vaginal examination revealed that the cervix was soft, small and not quite firm.

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

On June 25 there was no change in the patient's condition. The weight was 170 pounds. The blood pressure was 120 systolic, 80 diastolic. The blood sugar was 120 mg. per 100 cc.

On June 26 the patient again entered the hospital, and labor started about 3:00 a.m. on June 27. By 7:45 a.m. she was fully dilated and was delivered by a breech extraction of a 6 pound, 7 ounce, macerated fetus. The convalescence was uneventful.

The patient was seen in the office for a final check-up on July 25, when the weight was 162 pounds, the blood pressure 120 systolic, 70 diastolic, and the blood sugar 140 mg. per 100 cc. She was in excellent condition.

Comment: This case of diabetes developed, as many do, after a nervous shock—a thyroid operation. When first seen, the patient was approximately six months pregnant and had gained 10 pounds in one month. The extreme gain in weight at this stage of pregnancy suggested toxemia. The continued increase in weight for the next month was also suggestive. During this time the urine showed some albumin. The patient was sent to the hospital because there was some edema, a moderate rise in blood pressure and a large trace of albumin in the urine. Coincident with a drop in blood pressure to 120 systolic and a loss of 4 pounds in weight, the fetal heart sounds could not be obtained. The edema disappeared entirely, and the blood pressure returned to a normal level. After the baby died, one might have raised the question as to whether or not the patient should be delivered: such cases should always be left alone. The toxemia abated with the death of the baby, and the patient continued well until spontaneous labor started about six weeks later; she was delivered of a macerated fetus. This story is typical of diabetes; even under the best care toxemia may appear, and intrauterine death may follow.

"GREEN LIGHTS TO HEALTH"

I am talking to you today as a representative of the Massachusetts Medical Society to explain the purpose and character of a series of medical broadcasts that will come to you every Wednesday morning at 11:30. Each year since 1929 the physicians of Massachusetts in conjunction with the Massachusetts Department of Public Health have sponsored a series of health talks over the radio. This broadcasting station has donated the time as part of its contribution to the field of adult education. I should like at this time to express to the officials and personnel of Station WAAB our appreciation not only for the time on the air but also for the co-operation and encouragement they have given us these many years.

* "Green Lights to Health" broadcast given through Station WAAB by Dr. Gerald Hoeffel on Wednesday, November 13, and sponsored by the Public Education Committee of the Massachusetts Medical Society and the Massachusetts Department of Public Health.

In assuming the responsibility of this type of health education the medical society appreciates that these papers should be as stimulating and informative as possible. Physicians of Massachusetts prominent in the profession chosen to discuss the various phases of medicine in which they have an especial interest; thus they are well qualified to enlighten you concerning the commoner and more important diseases and injuries. We believe that the layman desires to know how to keep well and what to do when he is sick, and the papers will be presented from these points of view.

As a consequence, after listening to one of these programs, and especially to the series, one ought to gain very definite insight regarding the ever-changing knowledge and new advances in medicine.

One may ask why it is necessary for the physician to discuss over the air these matters of health and disease.

There are numerous evidences of interest on the part of the public in matters of medicine. Mr. Homer N. C. Ver, secretary of the American Museum of Health of recent New York World's Fair, in commenting on the public's interest in this great exhibition, has recently written, "The people thirst for knowledge about themselves. One has only to consider the popular health columns in the daily papers, the numerous popular-magazine articles, novels and biographies, and motion-picture scenarios based on medical fact or fancy to realize that this is true. As a matter of fact we all possess an innate curiosity and interest in medical science and practice. Only a very small group try to discourage or evade the teachings of the medical profession.

It is because the physicians of the State, represented by the Massachusetts Medical Society, recognize this universal interest on the part of the public that they take the opportunity of using the radio as a means of furthering medical education. We doctors believe that the future of medicine to a very great extent may be determined by the citizens of this country. If the public is ignorant, the practice of medicine will suffer; if they are informed, American medicine will continue to go forward.

Wherein do we find concrete examples of the public interest and responsibility in health matters? The public has assumed control of health matters by spending vast sums of money to maintain municipal, state and federal hospitals. The public has demanded that the health of its citizens be protected through medical supervision of water supplies, sewage control and the supervision of control of people handling food for public consumption. The public has instituted legislation governing the sale and distribution of drugs. In turn the public has demanded and obtained, with the help of the medical profession, protection from contagious diseases through the formulation of quarantine rules and regulations. The public, through its legislature, grants charters to medical schools so as to regulate the quality of medical education. To practice medicine its physicians must obtain licenses from the state. Finally, the public in its interest in health matters demands the right to choose its own physicians. These, then, are just a few of the many ways by which the public exerts its influence and interest in the field of medicine.

The doctor who recognizes the value of having his patient well informed practices medicine today differently than was customary years ago. In the old days the attitude on the part of the medical profession was that the patient should not be expected to be too well informed about the functions of the human body. The doctor's directions regarding illness were to be accepted as a command from a source enshrouded in the veil of mystery. That

passed a long time ago. The physician today recognizes that to obtain the quickest and most complete cure he must give to his patients an intelligent understanding of the underlying principles of medicine, the whys and wherefores of their sicknesses and resulting disabilities. This close relation between patient and physician really helps the patient to help himself. It also provides the doctor with detailed information that frequently aids him in helping his patient. This teamwork ultimately brings about the result that every patient seeks in consulting his doctor, namely, restoration to health and usefulness.

Hence it is obvious that a responsibility rests firmly on the shoulders of the layman if he is to obtain good medical advice from his family physician or public health official; that is, he must himself have a foundation of medical interest and knowledge that will serve him to judge how to obtain good medical advice and care.

One may say that a little knowledge is a dangerous thing; that a layman whose medical education exceeds his intelligence is apt to get into difficulty in the manner of self diagnosis, self medication or the development of neurosis and the like. This may be true of a small number of people, but they, like those who tamper with delicate machines without knowledge of them, soon learn that it is the best part of judgment to leave adjustments and repairs to the expert technician or mechanic. The same is true in regard to the human body. We all want to enjoy its use, know its possibilities for service and maintain it in a smoothly functioning order, but at the same time when there appears to be trouble we want it treated intelligently by a competent physician.

Intelligent people are eager to learn about important advances in medical knowledge. We as physicians believe that the layman has a right to know something about these new and better ways of treating certain common diseases and injuries. I repeat, with an understanding and knowledge of medical trends the layman is thereby placed in a better position to select good physicians to take care of him when he is sick.

We are prone to consider the field of medicine in too limited a way. We have perhaps put too much emphasis on that branch of medicine that deals with the diagnosis and treatment of actual disease at the expense of neglecting that other branch known as preventive medicine. This we know deals with the prevention of disease in three major ways: first, routine health examinations and the supervision of infants and children; second, the prevention of disease by means of immunization of the population against such important diseases as smallpox, diphtheria, typhoid fever, and so forth; and finally the prevention and spread of disease through isolation and quarantine regulations. In 1835 the vital statistics of Philadelphia revealed that the average expectation of life was twenty-one years. Preventive medicine carried on by doctors, mostly private practitioners in the United States, has raised life expectancy to above sixty years. We are not so aware of this important branch of medicine until there is a break in the system of public health activities interrupting and disabling the practice of preventive medicine. This tragic state of affairs exists in Europe today. Plagues, epidemics and infections that could be prevented have become rampant and will cause great and unnecessary loss of human life. Because of the great benefits from public health rules and regulations the layman must share in the responsibility of supporting and improving this great field of medical activity. This interest and support can come only from citizens who are informed and thus are aware of the vital importance of preventive medicine and public health control in their daily lives.

Time will not permit me to elaborate on the subject matter of each of these medical broadcasts that will be given. Included among them will be talks on the new advances in the treatment of pneumonia and of other infections, such as erysipelas, meningitis and tonsillitis and their complications. The importance and far reaching effects of diet and of vitamins will be analyzed, also the control of communicable diseases, mental health and the great field of preventive medicine and its bearing on the welfare of the entire nation.

You will be told about the family physician. We all recognize that the general practitioner is the backbone of medicine. It has been through his hard work and interest in his patients' health and happiness that progress in the medical world has been so marked. Many people do not realize how fast new knowledge is being added to the treatment of different diseases. This ever increasing knowledge pertaining to preventive medicine, diagnosis and treatment of diseased states has naturally increased the burden of the individual physician. As a result many doctors have been stimulated to limit their fields of activity to certain special branches of medical practice. Others have devoted full time to laboratory research.

Modern medicine today consists of a unity of these three important fields of medicine—the general practitioner, the specialist limiting himself to a certain branch of medicine and the medical research worker. The close relation between these three subdivisions allows for the interchange of knowledge that eventually is put into use for the benefit of the individual citizen. However, even the family physician or specialist as well as the layman must appreciate that, although the general principles of treatment remain the same, a doctor who practices only what he learned ten years ago—yes, even five years ago—may not be able to give his patient the best chance of recovery. Hence the goal of the medical profession and the rightful demand on the part of the patient is that the doctor in the community be sufficiently acquainted with the new knowledge to render treatment that will restore his patients to health and usefulness in the shortest possible time.

I am sure that by following this series of medical talks you will gain a knowledge of medicine in its broad aspects. You will be more appreciative of the part medicine plays in all life's daily activities. At work, at play, in the city or country, we are being continually influenced by discoveries, contributions and regulations coming from medical research and practice.

If you like these broadcasts write to Green Lights to Health, Station WAAB, Boston. If you do not understand some points in the broadcast write and ask about them. A reply will be sent. If you desire a mimeographed copy of the broadcast one will be sent if you will ask for it and send your name and address.

MEDICAL POSTGRADUATE EXTENSION COURSES

The following sessions given by the Medical Society in co-operation with the Department of Public Health the United States Health Service and the Federal Children's Bureau have been arranged for the week beginning

BARNSTABLE

Sunday, December 1 at 4:00 p.m.
Hospital, Hyannis Opera
educations and technic. In the
Dr. Donald E. Higgins

*BRISTOL NORTH

BRISTOL SOUTH (New Bedford Section)

Friday, November 29, at 4:00 p.m., at St. Luke's Hospital, New Bedford. Acute Abdominal Pain: Its interpretation and management. Instructor: Richard B. Cattell. Robert H. Goodwin, *Chairman*.

ESSEX NORTH

Friday, November 29, at 4:30 p.m., at the Clover Hill Hospital, Lawrence. Pediatric Case Discussions. Instructor: Joseph Garland. John Parr, *Chairman*.

ESSEX SOUTH

Tuesday, November 26, at 4:00 p.m., in the Conference Room, Salem Hospital, Salem. Chemotherapy in the Treatment of Gonococcal Infection. Instructor: Sylvester B. Kelley. J. Robert Shaughnessy, *Chairman*.

MIDDLESEX NORTH

Friday, November 29, at 5:00 p.m., at St. John's Hospital, Lowell. Technic and Treatment of Primary, Secondary and Tertiary Syphilis. Instructor: Rudolph Jacoby. William S. Lawler, *Chairman*.

PLYMOUTH

Tuesday, November 26, at 4:30 p.m., in the Nurses' Home of the Brockton Hospital, Brockton. Hemorrhage in Pregnancy, Labor and the Puerperium: Its diagnosis and treatment. Instructor: M. V. Kappius. Walter H. Pulsifer, *Chairman*.

*Because of Thanksgiving Day, the course will be omitted.

DEATHS

BRADY—CECIL N. BRADY, M.D., of Newton, died November 6. He was in his fifty-fourth year.

Born at Cannag, Nova Scotia, he received his degree from Tufts College Medical School in 1913. Dr. Brady was a former member of the Massachusetts Medical Society.

COX—CLYDE E. COX, M.D., of Worcester, died November 10. He was in his thirty-sixth year.

Born in St. Anthony, Idaho, he attended Leland Stanford University and received his degree from the Harvard Medical School in 1930. He served his internship at the Worcester City Hospital, where he later became an assistant physician.

He was a fellow of the Massachusetts Medical Society and the American Medical Association.

His widow, a daughter, his parents and a sister survive him.

EMERSON—FREDERICK L. EMERSON, M.D., of Boston, died November 10. He was in his eightieth year.

Born in Boston he attended English High School and received his degree from Boston University School of Medicine in 1892. Dr. Emerson was a former member of the staff of the Massachusetts Homoeopathic Hospital now the Massachusetts Memorial Hospitals, and was senior obstetrician of the Robinson Memorial Hospital, a part of the Massachusetts Memorial Hospitals. He had also served on the consulting staff of the Brooks Hospital, Brookline.

Dr. Emerson was a fellow of the Massachusetts Medical

Society and the American Medical Association and a member of the American Institute of Homeopathy.

His widow survives him.

HARVEY—WILLIAM W. HARVEY, M.D., of Boston, died November 10. He was in his seventy-fifth year.

Born in East Burke, Vermont, he attended Brown University and received his degree cum laude from the Harvard Medical School in 1898. Dr. Harvey was a member of the Massachusetts Medical Society and the American Medical Association and was one of the three founders of the Boston Club of Applied Psychology.

His widow and two daughters survive him.

MEAD—FREDERICK A. MEAD, M.D., of Chicopee, died November 14. He was in his seventy-second year.

Born in Gloversville, New York, he received his degree from Albany Medical College in 1892. After practicing a few years in upstate New York, he moved to Chicopee, where he practiced for forty-four years.

He was a member of the Massachusetts Medical Society and the American Medical Association.

CORRESPONDENCE

PHARMACEUTICAL RESEARCH

To the Editor: During the Pharmacopoeial Convention last May, a request was presented for the publication from time to time of research problems, which, if solved, would assist in the work of revision. To comply with this request the chairmen of subcommittees were requested to suggest subjects which in their special fields were particularly important.

The following subjects have been offered:

A method for biological assay of ergot that measures the content of both ergotoxine and ergonovine types of alkaloids.

An efficient and inexpensive method for biological assay of aconite and its preparations.

Statistical studies of the value of antipneumococcus serums in general practice.

A suitable standard of assay for Rheum based on its anthraquinone content.

The comparative anatomy of the rhizomes and roots of Chinese rhubarbs yielded by *Rheum officinale*, *R. palmatum*, *R. palmatum* var. *tanguticum* and hybrids between these and other *Rheum* species including *R. rhaponticum*.

Further studies of the assays of cantharides, ipecac and capsicum.

Chemical assay of aconite and aloë.

The separation of strychnine and brucine.

The therapeutic value of reduced iron.

The absorption of pure powdered electrolytic iron from the alimentary tract.

Rapid, accurate method for the determination of the pH of distilled water.

Further study of the limit of unsaturates test in cyclopropane.

Heavy metals' test for diluted hypophosphorous acid.

The sensitivity of the flame test for sodium in chemicals used as reagents (For example, potassium oxalate is required to 'impart no distinct yellow color to a colorless flame,' whereas with potassium nitrate a yellow flame is given by the presence of about 0.05 per cent sodium when testing a 5 per cent solution, and with potassium nitrate a yellow flame indicates about 0.02 per cent sodium when a 10 per cent solution is tested. Careful tests on sodium free salts to which known quantities of sodium salts are added would make possible a revision of the statements and might result in corrections.)

Oil of cassia, tests and constants

Oil of nutmeg, detection of pinene or redistilled oil of turpentine

Oil of peppermint, tests and constants (distinction between unrectified and rectified)

Stability of fluidextract of ergot

Tincture of digitalis a study of the U.S.P. tincture and a comparison of the tincture made from defatted drug to determine the difference if any, in activity

A cytogenetical study of *Rheum officinale* R. pal. matum and other Asiatic rhubarbs

A cytogenetical study of *Digitalis purpurea*

More detail will be given to anyone who is interested in investigating one of the subjects suggested

E FULLERTON COOK, Chairman
U.S.P. XII Revision

43rd Street and Woodland Avenue,
Philadelphia

NOTICES

BOSTON DOCTORS' SYMPHONY ORCHESTRA



The Boston Doctors' Symphony Orchestra will rehearse under Alexander Thiede, formerly concert master of the Cleveland Symphony Orchestra, every Thursday at 8:30 p.m. Those interested in becoming members should communicate with Dr. Julius Loman, Pelham Hall Hotel, Brookline (BEA 2430)

communicate with Dr. Julius Loman, Pelham Hall Hotel, Brookline (BEA 2430)

BOSTON LYING IN HOSPITAL

Dr. Austin W. Cheever will speak on 'Syphilis in Pregnancy' before the Journal Club at the Boston Lying in Hospital, on Wednesday, November 27, at 8:15 p.m. Physicians and medical students are cordially invited to attend.

BOSTON MEDICAL HISTORY CLUB

There will be a meeting of the Boston Medical History Club at the Boston Medical Library, 8 Fenway, on Monday, November 25, at 8:15 p.m. Dr. Robert W. Buck will speak on 'Eponyms in the History of Medicine'. All interested persons are cordially invited to attend.

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS, UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	ORTHOPEDIC CONSULTANT
Salem	December 2	Harold C. Bean
Haverhill	December 4	William T. Green
Lowell	December 6	Albert H. Brewster
Gardner	December 10	Mark H. Rogers
Brockton	December 12	George W. Van Gorder
Pittsfield	December 16	Francis A. Slowick
Hyannis	December 17	Paul L. Norton
Northampton	December 18	Garry deN. Hough, Jr.
Worcester	December 20	John W. O'Meara
Fall River	December 23	Eugene A. McCarthy

MASSACHUSETTS GENERAL HOSPITAL

A meeting of the Hospital Research Council will be held in the Ether Dome of the Massachusetts General Hospital, on Tuesday, November 26, at 5:00 p.m.

PROGRAM

- Salivary Conditioned Reflex in Psychoneurotic Patients
Drs. J. E. Finesinger, G. F. Sutherland and Miss F. McGuire
- Clinical Use of Electroencephalograms in the Localization of Intracranial Lesions
Dr. R. S. Schwab and Mrs. M. Thompson
- Cushing's Disease from the Point of View of a Hyperadrenocorticism Leading to Hyperglucocorticogenesis and Protein Deficiency Treatment based thereon
Drs. F. Albright and W. Parson

JOHN T. BOTTOMLEY SOCIETY

The regular monthly meeting of the John T. Bottomley Society will be held in the Out Patient Department Building of the Carney Hospital on Tuesday, November 26, at 11:30 a.m. Dr. Joseph A. Doherty will speak on 'Oral Surgery'.

Physicians and students are cordially invited to attend.

NEW ENGLAND DERMATOLOGICAL SOCIETY

The next regular meeting of the New England Dermatological Society will be held at the Boston City Hospital on Wednesday, December 4, at 2:00 p.m.

NEW ENGLAND OBSTETRICAL AND GYNECOLOGICAL SOCIETY

The twelfth annual meeting of the New England Obstetrical and Gynecological Society will be held in Boston on Wednesday, December 4. In the forenoon, clinics will be held at the Free Hospital for Women, Brookline, and the Boston City Hospital. A luncheon will be served at the University Club. In the afternoon, clinics will be held at the Carney Hospital and the Beth Israel Hospital. The annual dinner will take place in the evening at the University Club.

WALTHAM MEDICAL MEETING

There will be a clinicopathological conference of the Metropolitan State Hospital, Waltham, on Wednesday, November 27, at 8 p.m. A case of congenital juvenile taboparesis, complicated by rheumatic heart disease and

Streptococcus hemolyticus septicemia, will be presented by Drs. Clementine McKeon and Richard C. Wadsworth, and will be discussed by Dr. Harold E. MacMahon.

NORFOLK DISTRICT MEDICAL SOCIETY

A regular meeting of the Norfolk District Medical Society will be held at the Hotel Puritan, Boston, on Tuesday, November 26, at 8:30 p.m. Tel. KEN 1480.

PROGRAM

Business.

Symposium on Alcohol. Dr. Timothy Leary and Mr. Hermann C. Lythgoe.

Discussion to be opened by Dr. Merrill Moore.

Collation.

WACHUSETT MEDICAL SOCIETY

There will be a meeting of the Wachusett Medical Society at the Holden District Hospital on Wednesday, December 4, at 6:30 p.m.

PROGRAM

Case record. Drs. A. P. Skoog and Maurice Rubin.
Deficiency States and Anemia. Dr. William Dameshek.

Question period.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING SUNDAY, NOVEMBER 24

MONDAY, NOVEMBER 25

12:15-1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

*8:15 p.m. Eponyms in the History of Medicine. Dr. Robert W. Buck. Boston Medical History Club. Boston Medical Library, 8 Fenway.

TUESDAY, NOVEMBER 26

*9-10 a.m. X-ray Demonstration. Dr. A. Ettinger. Joseph H. Pratt Diagnostic Hospital.

*11:30 a.m. Oral Surgery. Dr. Joseph A. Doherty. John T. Bottomley Society. Carney Hospital.

12:15-1:15 p.m. Clinicoroentgenological conference. Peter Bent Brigham Hospital amphitheater.

5 p.m. Hospital Research Council. Massachusetts General Hospital.

WEDNESDAY, NOVEMBER 27

*9-10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*12 m. Clinicopathological conference. Children's Hospital.

*2-4 p.m. Hematuria and Dysuria. Drs. W. C. Quinby and E. A. Stead. Peter Bent Brigham Hospital.

*8:15 p.m. Syphilis in Pregnancy. Dr. Austin W. Cheever. Journal Club. Boston Lying-in Hospital.

FRIDAY, NOVEMBER 29

*9-10 a.m. Marble Bone Disease. Dr. Albert Frank. Joseph H. Pratt Diagnostic Hospital.

SATURDAY, NOVEMBER 30

*9-10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*Open to the medical profession.

NOVEMBER 22 — Salem Tumor Clinic. Page 831, issue of November 14.

NOVEMBER 27 — Waltham Medical Meeting. Page 875.

DECEMBER 4 — New England Dermatological Society. Page 875.

DECEMBER 4 — Wachusett Medical Society. Notice above.

DECEMBER 4 — New England Obstetrical and Gynecological Society. Page 875.

DECEMBER 8-11 — American Academy of Dermatology and Syphilology. Page 831, issue of November 14.

DECEMBER 10 — New England Society of Anesthesiology. Page 743, issue of October 31.

DECEMBER 12 — Pentucket Association of Physicians. Page 263, issue of August 15.

DECEMBER 27-29 — National Convention of the Association of Medical Students, Boston.

JANUARY 4, 1941 — American Board of Obstetrics and Gynecology. Page 787, issue of November 7.

MARCH 8 — American Board of Ophthalmology. Page 201, issue of August 1.

APRIL 21-25 — American College of Physicians. Page 1065, issue of June 20.

MAY 21, 22 — Massachusetts Medical Society, Boston.

JUNE 2-6 — American Medical Association. Cleveland, Ohio.

DISTRICT MEDICAL SOCIETIES

ESSEX SOUTH

DECEMBER 4-MAY 14 — Page 831, issue of November 14.

JANUARY 8 — Visceral Pain and Its Relief. Dr. James C. White. Dunbar State Hospital, Hathorne.

FEBRUARY 5 — Subject to be announced. Lynn Hospital.

MARCH 5 — X-ray in Heart Disease. Dr. Merrill C. Sosman. Essex Sanatorium, Middleton.

APRIL 2 — Pediatric Problems in General Practice. Dr. Joseph Garland. Addison Gilbert Hospital, Gloucester.

MAY 14 — Relation of the Doctor to the Law. Mr. Leland Powers. New Ocean House, Swampscott.

FRANKLIN

JANUARY 14.

MARCH 11.

MAY 13.

Meetings will be held at 11 a.m. at the Franklin County Hospital, Greenfield.

NORFOLK

NOVEMBER 26 — Notice above.

JANUARY 28 — Carney Hospital.

FEBRUARY 25 — Medico-Legal meeting. 8:30 p.m. Hotel Puritan, Boston.

MARCH 25 — To be announced.

MAY 8 — Censors' meeting. Hotel Puritan.

SUFFOLK

JANUARY 29 — Page 604, issue of October 10.

APRIL 30 — Page 604, issue of October 10.

WORCESTER

DECEMBER 11 — St. Vincent Hospital, Worcester.

JANUARY 8, 1941 — Worcester City Hospital, Worcester.

FEBRUARY 12 — Worcester State Hospital, Worcester.

MARCH 12 — Memorial Hospital, Worcester.

APRIL 9 — Hahnemann Hospital, Worcester.

Supper at 6:30 p.m. followed by a business meeting and scientific program.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

The 1940 Year Book of Public Health. Edited by J. C. Geiger, M.D., Dr.P.H., director of public health, City and County of San Francisco; clinical professor of epidemiology, University of California Medical School. 12^o, cloth, 560 pp., with 12 figures and 24 tables. Chicago: Year Book Publishers, 1940. \$3.00.

Vitamin Therapy in General Practice. By Edgar S. Gordon, M.A., M.D., associate in medicine and instructor in physiological chemistry, University of Wisconsin Medical School, and Elmer L. Sevringhaus, M.D., professor of medicine, University of Wisconsin Medical School. 8^o, cloth, 258 pp., with 35 illustrations. Chicago: Year Book Publishers, Inc., 1940. \$3.25.

The New England Journal of Medicine

Copyright, 1940, by the Massachusetts Medical Society

VOLUME 223

NOVEMBER 28, 1940

NUMBER 22

SULFATHIAZOLE THERAPY OF *STAPHYLOCOCCUS AUREUS* BACTEREMIA*

CHARLES H. RAMMELKAMP, M.D.,† AND CHESTER S. KEEFER, M.D.‡

BOSTON

STAPHYLOCOCCUS AUREUS bacteremia is always a grave disease. The mortality reported in large series of cases varies from 68 per cent¹ to 89 per cent.² Recently Mendell³ reported 35 cases, with a fatality rate of 83 per cent, and Skinner and Keefer⁴ found a mortality rate of 82 per cent in the study of 122 cases observed at the Boston City Hospital. These reports, which are based on large numbers of cases, serve to emphasize the need for a new therapeutic approach to this disease.

With the introduction of the thiazole derivatives of sulfanilamide by Fosbinder and Walter,⁵ it soon became evident that these drugs would prove useful in the treatment of infections. Recent studies have shown that the thiazole derivatives inhibited the growth of *Staph. aureus* in broth,^{6,7} and in urine.⁸ Rammelkamp and Keefer⁹ showed that when sulfathiazole was added to defibrinated whole blood in vitro there was a marked increase in the bactericidal and bacteriostatic action against pathogenic staphylococci. Further, it was determined that a concentration of between 2.5 and 5 mg. per 100 cc. of blood was necessary to obtain the maximal effect. Comparison of the bactericidal action of sulfathiazole, sulfamethylthiazole, sulfapyridine and sulfanilamide against *Staph. aureus* showed sulfathiazole to be slightly superior to the other drugs named. In experimental staphylococcal infections in mice, sulfathiazole prolongs the life of the animal.^{10,11}

Recently several cases of *Staph. aureus* bacteremia in which the patient recovered following treatment with sulfathiazole or sulfamethylthiazole have been reported.¹²⁻¹⁸ These reports are encouraging, but to evaluate the effectiveness of

sulfathiazole therapy in the treatment of staphylococcal bacteremia, it is necessary to analyze both successes and failures. For this reason the following study of 7 cases of *Staph. aureus* bacteremia treated with sulfathiazole[§] is reported. In addition an investigation was made of the bactericidal properties of the blood obtained from 3 of these patients and from normal persons following the administration of sulfathiazole by mouth.

CASE REPORTS

CASE 1 (Bacteremia with death). A 62-year-old, married woman complained of cough and pain in the right chest. About a month before admission to the hospital she developed a cough that was productive of small amounts of cream-colored sputum. The cough gradually decreased up to the time of admission. Three days before entry she developed a "dagger-like" pain in the right chest that radiated to the precordium. This pain was constant, and it was aggravated by motion, deep breathing and coughing. There was no history of chills or previous staphylococcal infection. For several years she had experienced some dyspnea on exertion. There had been no recent weight loss or symptoms referable to the urinary tract.

On admission the temperature was 100.4°F., the pulse 84 and the respirations 24. The patient was overweight, but she did not appear acutely ill. The skin was dry and clean. The pharynx was not injected. In the lower jaw a few carious teeth were noted. The tongue was smooth and moist. Ophthalmoscopic examination revealed nothing abnormal. There was no lymphadenopathy. Chest expansion was good. On percussion there was dullness over the right lower lobe posteriorly, and over this area a few rales could be heard. The heart was not enlarged, and the sounds were of good quality. The blood pressure was 146/74. Examination of the abdomen revealed nothing abnormal. The reflexes were physiologic.

Laboratory examinations showed the urine to be clear and normal. The hemoglobin was 76 per cent, the red-cell count 3,960,000, and the white-cell count 18,000. A blood Hinton test was negative, the nonprotein nitrogen 22 mg. per 100 cc. Examination of the sputum failed to reveal any pneumococci. An x-ray film of the chest on admission showed some infiltration of the right lower lobe.

§We are indebted to Dr. George Harrop of E. R. Squibb and Sons, New York City, for generous supplies of sulfathiazole.

*From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard), Boston City Hospital, and the Department of Medicine, Harvard Medical School, Boston.

†Assistant in medicine, Boston University School of Medicine; resident physician, Evans Memorial, Massachusetts Memorial Hospitals.

‡Assistant in medicine, Boston University School of Medicine; director, Evans Memorial, and physician-in-chief, Massachusetts Memorial Hospitals.

The clinical course of this patient's illness is shown in Figure 1. At first, it was thought that the patient had a pneumonic process in the right lower lobe, and therefore she was given sulfapyridine. The blood culture taken on the day after admission was positive for *Staph. aureus*. After 1 week of fever the temperature returned to normal

days of this therapy the blood remained sterile, then again became positive. Because of nausea and failure to sterilize the blood stream sulfathiazole was omitted during the 7th week, to be resumed later in smaller doses. During the last 5 weeks the blood cultures remained sterile and the patient gradually improved. On discharge to co-

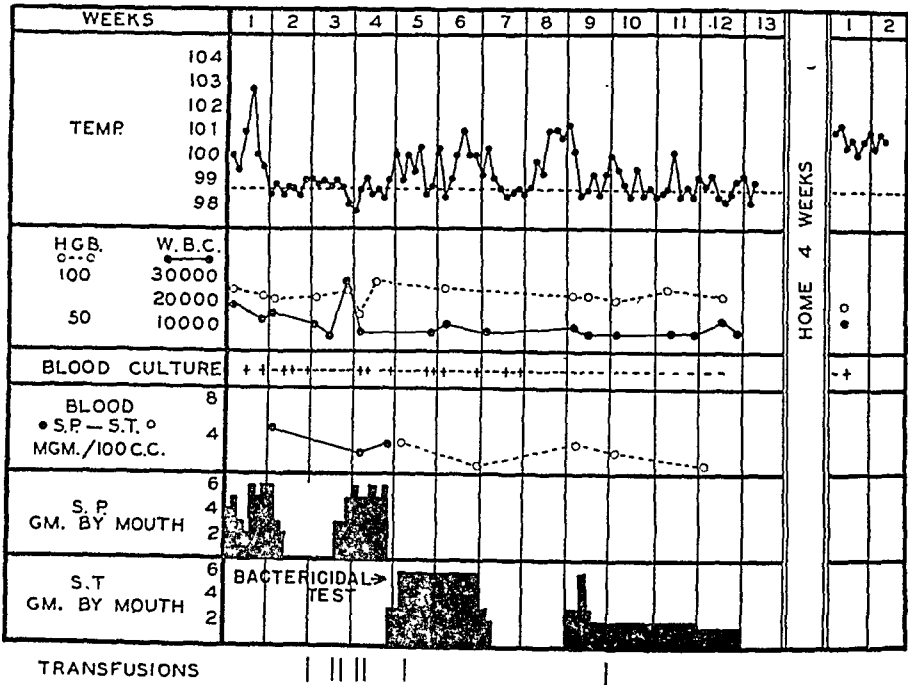


FIGURE 1. *Staphylococcus aureus* Bacteremia with Death.
S.T. = sulfathiazole; S.P. = sulfapyridine.

and the sulfapyridine was discontinued. Nevertheless, the blood continued to show *Staph. aureus* on culture. Sulfapyridine therapy was then resumed. Investigation as to the cause of the bacteremia failed to reveal a focus

valesce at home she had no complaints other than a aching pain in the back and some weakness. She remained at home in bed for 4 weeks and then re-en the hospital in a critical condition. She was unre-

TABLE 1. Bactericidal Effect of Defibrinated Blood on *Staphylococcus aureus* before and Two Hours following Administration of 4 Gm. of Sulfathiazole.

BLOOD	FACTOR	DILUTION OF CULTURE							
		10 ⁻¹	10 ⁻²	10 ⁻³	10 ⁻⁴	10 ⁻⁵	10 ⁻⁶	10 ⁻⁷	10 ⁻⁸
Case 1*	Before S.T.	Hemolysis	+++	+++	0	0	0	0	0
	Colonies per cc.	700	550	55	76	60			
After S.T.	Hemolysis	+++	0	0	0	0	0	0	0
	Colonies per cc.	1,800	450	30	0	0	0	0	0
Case 2†	Before S.T.	Hemolysis	+++	+++	+++	+++	+++	0	0
	Colonies per cc.	700	550	55	76	60			
After S.T.	Hemolysis	+++	+	0	0	0	0	0	0
	Colonies per cc.	1,400	24	0	0	0	0	0	0
Case 3‡	Before S.T.	Hemolysis	+++	+	0	0	0	0	0
	Colonies per cc.	700	550	55	76	60			
After S.T.	Hemolysis	+++	0	0	0	0	0	0	0
	Colonies per cc.	160,000	10,000	25,000	2,090	400	576		

*Case 1. Concentration of sulfapyridine was 3.5 mg. per 100 cc. of blood before administration of sulfathiazole; the 10⁻⁸ dilution of the culture contained 4 organisms per cubic centimeter.
†Case 2. Concentration of sulfanilamide was 5.7 mg. per 100 cc. of blood before administration of sulfathiazole; the 10⁻⁸ dilution of the culture contained 3 organisms per cubic centimeter.
‡Case 3. Concentration of sulfapyridine was 10.4 mg. per 100 cc. of blood before administration of sulfathiazole; the 10⁻⁸ dilution of the culture contained 21 organisms per cubic centimeter.

other than the pulmonary infiltration. X-ray films of the spine, pelvis and gall bladder and an intravenous pyelogram were interpreted as normal. At the end of the 4th week in the hospital the patient again had fever, and at this time sulfathiazole was started. During the first 3

sive, and no history could be obtained from her. However, it was learned that a week before entry she had begun to complain of pain in the back and high fever. Examination showed an injected pharynx. There were abnormal findings in the chest. A soft systolic murmur

was heard over the apex of the heart; the blood pressure was 140/70. The abdomen was soft, and no masses could be felt. There was bilateral ankle clonus and a doubtful Babinski sign on the right side.

Laboratory examinations showed a hemoglobin content of 60 per cent and a white-cell count of 14,500. The nonprotein nitrogen was 23 mg. per 100 cc. A lumbar puncture showed an initial pressure of 230 mm. of water, with normal dynamics. The fluid was xanthochromic, contained no cells and had an increased protein content. An x-ray film of the spine revealed a collapsed 11th dorsal vertebra. Over this vertebra marked tenderness was noted. The blood culture was again positive for *Staph.*

maintained sterile, and the patient was discharged home. She remained in bed and during the week before re-entry had a recurrence of fever and complained of pain in the back. On admission she showed signs of spinal-cord compression. X-ray films revealed a collapse of the 11th dorsal vertebra. Blood culture was again positive for *Staph. aureus*. The patient expired 8 days later, the diagnosis being osteomyelitis of the 11th dorsal vertebra, extradural abscess and *Staph. aureus* bacteremia.

This patient was treated with blood transfusions and chemotherapy, and although an increase in the bactericidal power of the blood after the administration of sulfathiazole was demonstrated in a test against the patient's

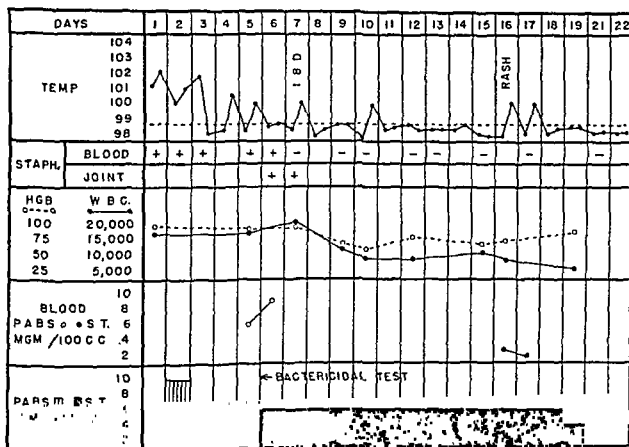


FIGURE 2. *Staphylococcus aureus* Bacteremia with Recovery.

P.A.B.S. = sulfanilamide; S.T. = sulfathiazole.

The positive blood culture on the sixth hospital day was taken before sulfathiazole was administered. The blood culture on the seventh day was taken before incision and drainage of the abscess.

aureus. The patient remained stuporous and expired on the 8th hospital day. Permission for a post-mortem examination could not be obtained.

Comment. This 62-year-old woman had signs of pulmonary infiltration, and the blood contained *Staph. aureus* on culture. No focus of infection other than the lesion in the lung could be found during the first admission. During the 1st month the patient was given sulfapyridine but the blood cultures remained positive. At the end of the 4th week in the hospital, sulfathiazole therapy was instituted, at which time a bactericidal test was done. Table 1 shows the results of this test. It can be seen from this table that the blood taken 2 hours after administration of 4 gm. of sulfathiazole showed an increase in the bactericidal power as compared to that of the blood taken before the test and containing sulfapyridine alone. For 3 days after the institution of sulfathiazole therapy the blood cultures were sterile, but later they again became positive. Because of the continued fever and some nausea, the drug was discontinued, to be readministered in smaller doses 10 days later. Gradually the temperature became lower, the blood cultures re-

mained sterile, the blood did not remain sterile. Important in the fatal outcome of this case was the development of a metastatic lesion that was not amenable to surgical drainage.

CASE 2 (Bacteremia with recovery). A 27-year-old man entered the hospital because of pain in the right sterno-clavicular joint. About a week before admission he had had an acute upper-respiratory infection; otherwise he had been in good health. Three days later he awoke early in the morning because of severe pain in the right sterno-clavicular region. The joint became swollen and tender, and the pain was so severe that he remained in bed. The patient also had sensations of chilliness and sweating. Ten years previously he had had gonorrhea, but he denied any recent exposure to infection.

The temperature was 100.8°F., the pulse 110, and the respirations 24. The patient appeared well-nourished and had a warm, moist skin without eruptions. The tongue was dry and coated; the teeth were carious. The lung fields were clear. The heart was of normal size and the sounds were of good quality. The spleen and liver could not be palpated, and the prostate felt normal. There were

tenderness, hyperemia, swelling and induration over the right sternoclavicular joint. Movement of the joint caused severe pain.

Laboratory examination revealed that the urine was clear and normal. The white-cell count was 17,400, and the hemoglobin 94 per cent. Blood Hinton and gonococcal complement-fixation tests were negative.

Figure 2 shows the clinical course of the disease. Because of the involvement of the sternoclavicular joint and a history of a previous gonococcal infection, it was thought at first that gonococcal arthritis was the most likely diagnosis. Therefore, the patient was given sulfanilamide as indicated on the chart. On the 5th hospital day the blood culture taken on the day of entry was reported to

the left hip joint. Eight days before admission he had fallen on the ice while skating, and although the hip was tender for a short time, he noticed no pain for 3 days. On the 4th day following the injury the left leg felt stiff, and that night he was awakened by a sharp, steady pain in both hips, which was severer on the left side. The pain was so intense that he had to remain in bed until the time of entry. The past history revealed that he had had several boils on his neck during the month or two before entry.

Physical examination showed a boy who appeared acutely ill. Both pupils reacted to light and accommodation, but the right pupil was slightly dilated. The heart rate was rapid, and there was a soft systolic murmur at

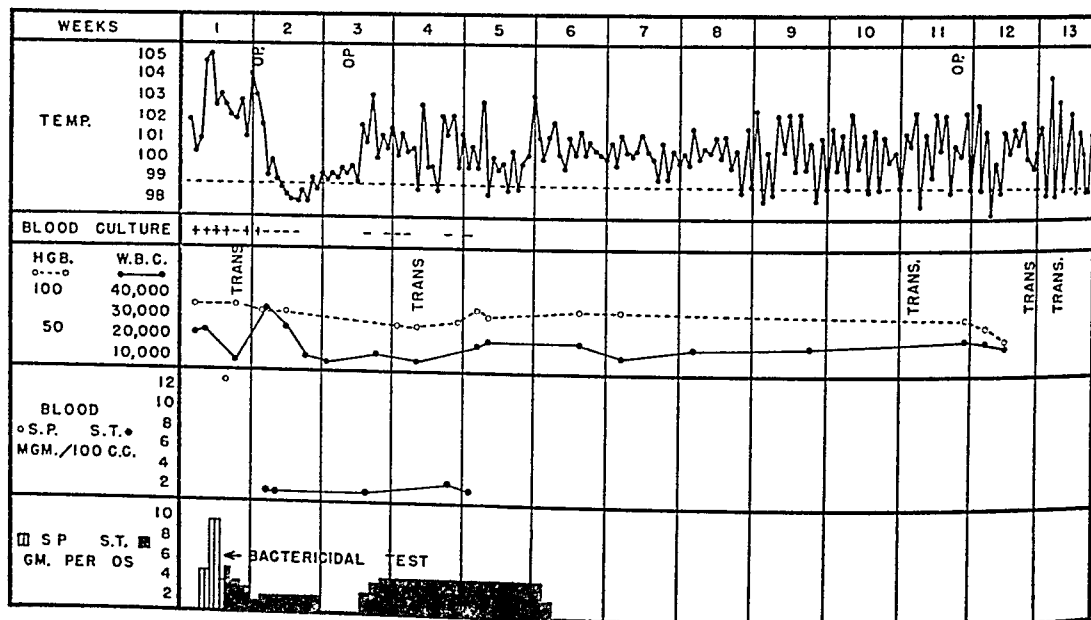


FIGURE 3. *Staphylococcus aureus* Bacteremia with Death.
S.P. = sulfapyridine; S.T. = sulfathiazole.

be positive for *Staph. aureus*. The patient was then given 6 gm. of sulfathiazole daily. The blood showed an increased bactericidal effect, and the cultures became sterile. On the 7th hospital day the joint was incised and drained. Cultures of the pus showed *Staph. aureus*. On the 16th hospital day the patient developed a generalized maculopapular rash and sulfathiazole was discontinued. He was discharged well on the 22nd hospital day.

Comment. A 27-year-old man with a staphylococcal infection of the sternoclavicular joint and invasion of the blood stream was treated with sulfanilamide, sulfathiazole, and incision and drainage of the local infection. He made an uneventful recovery. During the treatment with sulfathiazole some anemia was noted, and on the 11th day after the institution of sulfathiazole the patient developed fever and a generalized skin rash. The fever and rash subsided immediately after withdrawal of the drug. A bactericidal test (Table 1) was done on the patient's blood while he was receiving sulfanilamide and again 2 hours after the administration of 4 gm. of sulfathiazole. The second specimen of blood showed a marked increase in the bactericidal effect against the strain of *Staph. aureus* that had been isolated from the blood stream of this patient.

CASE 3 (Bacteremia with death). A 17-year-old boy entered the hospital complaining of pain in the region of

the apex. Abdominal examination revealed nothing abnormal; the spleen could not be felt. There were pain and tenderness on pressure over the left sacroiliac joint, but neither redness nor swelling was noted.

Laboratory examination showed a red-cell count of 4,200,000, with a hemoglobin of 85 per cent. The white-cell count was 20,500. The urine was normal. A blood Hinton test was negative. Lumbar puncture revealed a normal spinal fluid with no increase in cells. X-ray films of the hips and chest on admission showed nothing abnormal.

The clinical course of this patient's illness is shown in Figure 3. *Staph. aureus* was obtained on culture of the blood, and sulfapyridine was started immediately. On the 3rd hospital day there were 39 colonies of staphylococci per cubic centimeter of blood. On the 5th day sulfathiazole was administered, and on the following day the culture was sterile. The next two cultures, on the 7th and 8th days, were positive, but 1-cc. and 2-cc. pour plates showed no growth. Roentgenograms of the sacroiliac region were repeated, and they showed some destruction of the left sacroiliac joint. On the 8th hospital day the joint was drained, and cultures taken from the pus at the time of operation showed staphylococci. Following operation the temperature fell to normal and the blood cultures became sterile. In the 3rd week, following the removal

f the pack, the patient again began to show irregular fever. The cultures of the blood were sterile, but because of the fever sulfathiazole was again administered. Metastatic abscesses were searched for, but none were found. During the 11th week the left sacroiliac region was reexplored and after chiseling through the lower part of the joint a large pocket of pus was found. Because considerable bleeding was encountered, the joint was packed lightly. However, the patient continued to lose considerable blood from the wound, and during removal of the pack a few days later, severe bleeding occurred. Transfusions were given but the bleeding did not stop. The patient died following a severe hemorrhage from the wound. Permission for a post mortem examination was not obtained.

Comment This 17-year-old boy had a staphylococcal infection of the left sacroiliac joint. Cultures of the

coughing, and he began to perspire profusely and feel weak. These symptoms increased progressively until the time of admission. He had also noticed a foul odor around the upper portion of the cast.

Physical examination revealed a patient appearing critically ill. The respirations were 28. The skin was warm and moist. On percussion there was dullness over the right lower lung field posteriorly, and over this area rhonchi and coarse rales were heard. A few rales and diminished breath sounds were noted over the left base. The ribs were tender to pressure on both sides. The heart was not enlarged; no murmurs were heard; the rate was 140. The abdomen was normal. Around the upper portion of the cast a foul odor was noted, and pus could be seen oozing from the upper pinhole.

Laboratory examination revealed a red-cell count of 5,080,000. The white-cell count was 9,800, with 86 per

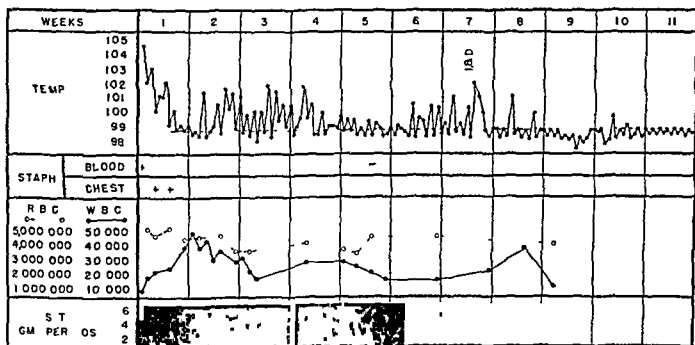


FIGURE 4. *Staphylococcus aureus* Bacteremia with Recovery
ST = sulfathiazole

blood were positive for *Staph. aureus*. Under sulphyridine therapy the cultures remained positive. When sulfathiazole therapy was instituted, a bactericidal test was done. The results of which are shown in Table I. The increase in bactericidal effect in this experiment following the administration of 4 gm. of sulfathiazole by mouth was not so marked as it was in Cases 1 and 2 but some increase was noted. The blood stream was not completely sterilized by sulfathiazole, however, the pour plates showed a decrease in the number of organisms per cubic centimeter of blood. Local drainage was followed by a fall in temperature to normal and by sterilization of the blood stream. After removal of the pack in the 3rd week of illness the temperature again became elevated but the blood cultures remained sterile. Sulfathiazole had no apparent effect on the fever at this time. In the 11th week of illness exploration revealed another large cavity filled with pus. The patient died shortly after this operation as a result of severe hemorrhage from the wound.

CASE 4 (Bacteremia with recovery) A 40-year-old man entered the hospital with the complaint of pain in the chest and chills. A month previously he had been admitted because of a fractured right femur for which he had a Roger-Anderson reduction. Two weeks later the pins were removed and the patient was discharged home to convalesce. About a week before the present entry he began to have pain in the chest, which was aggravated by

cent polymorphonuclear neutrophils. The urine showed a + reaction for sugar, and the sediment contained a few red blood cells and white blood cells. A blood Hinton test was negative. The nonprotein nitrogen was 29 mg. per 100 cc.

The clinical course of this patient is shown in Figure 4. After a blood culture was taken the patient was started on sulfathiazole therapy. An x-ray film of the chest on admission showed infiltration at the left base. The patient was known to have diabetes but it was well controlled on 5 to 15 units of insulin daily. On the 3rd day in the hospital he developed signs of fluid at the left base, a thoracentesis was done, the culture of fluid showing *Staph. aureus*. A second culture of the chest fluid on the 5th day yielded the same organism. On the 7th day the cast was removed and the patient placed in a Thomas splint. Under therapy with sulfathiazole the cultures of the blood and of the chest fluid became sterile, but the patient continued to have a low grade fever and leukocytosis. Sulfathiazole was discontinued during the 6th week in the hospital and shortly thereafter the temperature increased. X-ray films at that time showed changes consistent with osteomyelitis of the proximal fragment of the femur. In the 7th week more adequate drainage was established, and thereafter the temperature gradually returned to normal.

Comment A 40-year-old man developed a staphylo-

coccal bacteremia and empyema following a fracture of the right femur. Sterilization of the blood stream and empyema followed sulfathiazole therapy. Later, after the establishment of adequate drainage of the focus of osteomyelitis, the temperature returned to normal, and he recovered.

CASE 5 (*Bacteremia with death*). A 59-year-old man entered the hospital complaining of pain in the left leg. Seven weeks before admission he slipped and fell on the left knee, and several nights later it began to swell and became painful. However, he continued his work as a longshoreman. Three weeks before admission to the hospital the knee became stiff and the pain grew much worse. In addition, for 1 week prior to admission he had noted some aching in the right shoulder. No further history could be obtained.

On admission the temperature was 99°F., the pulse 100, and the respirations 28. The skin was dry, pale and warm. The lower teeth were carious, and the pharynx was injected. The trachea was in the midline. Dullness, harsh breath sounds and rhonchi were present over the apices posteriorly on both sides. The heart was not enlarged; the rhythm was regular, and no murmurs were heard. The spleen was not enlarged, and no masses were palpated in the abdomen. The left knee was swollen, and there was redness over the lateral portion of the knee and the upper tibia. Fluctuation was present, and motion of the joint caused pain.

Laboratory examination showed a urine with a specific gravity of 1.022, a trace of albumin and a positive test for acetone. The sediment showed a moderate number of white blood cells. The red-cell count was 3,300,000, the white-cell count 13,600, and the hemoglobin 72 per cent. Sputum examination revealed no acid-fast organisms. Two stool examinations gave a positive guaiac test for blood.

A short time after admission the patient coughed up a considerable amount of blood; it was impossible to tell whether it came from the stomach or the lungs. The hemoglobin fell to 40 per cent, and the patient was given a transfusion. Cultures of the blood and of the fluid aspirated from the knee joint showed *Staph. aureus*. The knee was incised and drained on the 3rd hospital day. X-ray films of the knee showed erosion of the lateral aspect of the tibia. On admission the patient was given sulfapyridine, but on the 4th hospital day this was changed to sulfathiazole. The temperature was subnormal until it rose to 101°F. terminally. He died on the 7th day in the hospital.

Comment. In summary, this 59-year-old man entered the hospital with pyogenic arthritis of the left knee, osteomyelitis of the tibia, signs of consolidation in the lung and a blood-stream infection due to *Staph. aureus*. Soon after admission he had a severe hemorrhage from the mouth. In spite of transfusions, sulfapyridine therapy for 4 days and sulfathiazole for 3 days, he expired on the 7th hospital day.

CASE 6 (*Bacteremia with death*). A 47-year-old woman entered the hospital complaining of pain in the right knee joint. Four days before admission she developed a shaking chill and noticed pain in the right knee joint, which was aggravated by motion. Soon after the chill there was slight swelling in the knee joint.

There was no history of previous staphylococcal infection. For several days she had noticed slight urinary frequency, and nocturia with dysuria. A mild cough had been present, which was productive only of whitish sputum.

Physical examination revealed a very obese woman with a temperature of 105°F., a pulse of 128 and respirations

of 40. The skin was warm and moist; no eruptions were noted. The tongue was coated. The pharynx was not injected. Chest expansion was equal on both sides. The trachea was in the midline. Dullness to percussion was present over the left base, without changes in breath sounds. A few scattered rales were heard at the right base. No tenderness or masses were noted in the abdomen. The right knee was swollen slightly, but there was no local redness or signs of fluctuation. Marked pain was caused by motion of the knee.

Laboratory examination revealed that the urine was normal except for a trace of albumin and numerous white cells in the sediment. The hemoglobin was 87 per cent, and the white-cell count 10,200; blood Hinton and gonococcal complement-fixation tests were negative. The non-protein nitrogen was 30 mg. per 100 cc. An electrocardiogram was reported as normal. Sputum examination showed no pneumococci.

The patient was treated symptomatically. On the 3rd day the temperature was still elevated, the knee was markedly swollen and somewhat red, and questionable fluctuation was present. A chest film on the 3rd day showed patchy infiltration at both bases. An x-ray film of the knee joint revealed narrowing of the joint space and swelling of the soft tissues. No bony changes were noted. On the 5th day the cultures of the blood were reported as containing *Staph. aureus*. The patient was started on sulfathiazole, 6 gm. daily, at this time. Before the knee joint could be drained she died.

Comment. This 47-year-old woman was admitted to the hospital with symptoms of pyogenic arthritis of the right knee. *Staph. aureus* had invaded the blood stream, and there was x-ray evidence of metastatic lesions in the lung. Sulfathiazole therapy was instituted, but the patient expired 24 hours later.

CASE 7 (*Bacteremia with recovery*). A 13-year-old boy entered the hospital because of severe pain in the right forearm. Three days before admission a streetcar door closed on his right arm. The next day he began to complain of pain in this area. The mother noticed at this time that the arm was swollen and tender. There was no previous history of staphylococcal infections.

Physical examination showed redness, swelling and local tenderness over the lower third of the right radius. The lymph nodes in the right axilla were slightly enlarged. The lungs were resonant to percussion, and no rales were heard. Auscultation of the heart revealed nothing abnormal. The liver and spleen were not palpable.

Laboratory examination showed a normal urine. The white-cell count was 13,600, and the red-cell count 4,120,000, with a hemoglobin concentration of 85 per cent. Roentgenograms revealed destruction of the distal end of the right radius, with marked soft-tissue swelling in this area.

Soon after admission the boy had a chill, the temperature reaching 103°F. Blood withdrawn during the chill was cultured and showed *Staph. aureus*. The day after entry the area of osteomyelitis was drained. Cultures of the pus showed *Staph. aureus*. The wound was packed with vaseline gauze and a posterior splint applied. Sulfathiazole was administered in a dosage of 0.75 gm. every 4 hours. The concentration of the drug in the blood varied from 1.8 and 5.1 mg. per 100 cc.

Following operation the temperature remained slightly elevated and two blood cultures showed *Staph. aureus*. Because of the low-grade fever and positive blood cultures the vaseline pack was removed on the 13th postoperative day. The temperature immediately returned to normal.

and the blood cultures became sterile. Ten days after the institution of chemotherapy the conjunctivas became infected. Several days later a lesion simulating erythema nodosum appeared over the lower extremities. Sulfathiazole was discontinued, and the skin lesions rapidly disappeared.

Comment. A 13-year-old boy had osteomyelitis of the radius and staphylococcal bacteremia. The clinical course of the illness was especially interesting. Drainage of the localized abscess failed to sterilize the blood stream and in addition, the temperature remained elevated. It was not until the vaseline pack had been removed and adequate drainage established that the patient recovered.

BACTERICIDAL STUDIES FOLLOWING THE ADMINISTRATION OF SULFATHIAZOLE BY MOUTH

Methods

The bactericidal tests here reported were carried out following a technic described in a previous publication.⁹ The organisms used were isolated from the blood stream of Cases 1, 2 and 3 and from a case of osteomyelitis of the rib. All strains

the administration of the drug. Each blood sample was defibrinated, and 0.5-cc amounts were placed in eight pyrex test tubes. To each of these tubes 0.1 cc of a saline dilution, ranging from 10^{-1} through 10^{-8} of the sixteen hour peptone broth culture, was added. The tubes were sealed in a gas-oxygen flame and rotated in the incubator at 37°C for forty-eight hours. The tubes were then examined for hemolysis, those showing no hemolysis were plated out and the colonies counted. The number of organisms contained in the original inoculum was calculated from the number of organisms contained in 0.25 cc of the fluid in the eighth tube. The concentration of the drug in the blood was determined at the time of withdrawal of the specimens.

Results

Figure 5 shows in a graphic form the results observed following the administration of 4 gm

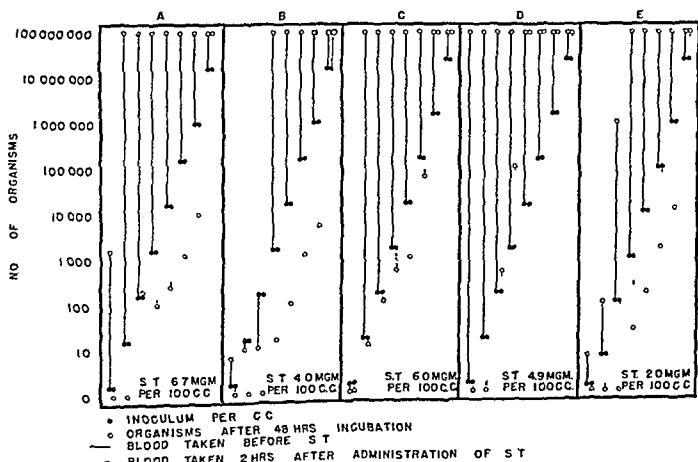


FIGURE 5 Bactericidal Effect on *Staphylococcus aureus* in Normal Defibrinated Blood following the Oral Administration of 4 Gm of Sulfathiazole
ST = sulfathiazole

produced yellow pigment on blood agar and also gave a positive coagulase reaction. The organisms were stored on blood agar slants, and sixteen hour peptone broth cultures were used in all experiments.

Each patient (Cases 1, 2, 3) and all the normal subjects used in this study were given 4 gm of sulfathiazole by mouth. Under sterile precautions, venous blood was withdrawn before the administration of sulfathiazole and again two hours after

of sulfathiazole by mouth to 5 normal persons. In general, if the original inoculum was 1,000,000 organisms per cubic centimeter or less, a bactericidal effect was demonstrable after forty-eight hours incubation. Experiment D is an exception to this statement. Here, when the original inoculum was over 20 organisms per cubic centimeter, no bactericidal effect was observed. However, bacteriostasis was demonstrated. This cannot be explained by a low level of sulfathiazole in the

blood, since the concentration here was more than twice the concentration in Experiment E. Rather, it appears that blood capable of producing some bacteriostasis normally will exhibit even more marked bacteriostasis and bactericidal action following the administration of sulfathiazole by mouth.

In the experiments performed with the bloods of patients with *Staph. aureus* bacteremia against their own organisms, each sample contained either sulfanilamide (Case 2) or sulfapyridine (Cases 1 and 3) at the time these tests were carried out. The concentration of the various drugs in the blood before the administration of sulfathiazole is recorded in Table 1. In all three cases there was an increase in the bactericidal effect following the administration of sulfathiazole; this was most marked in the patient that was already receiving sulfanilamide (Case 2).

COMMENT

Seven cases of *Staph. aureus* bacteremia were treated with sulfathiazole; 3 recovered (Cases 2, 4 and 7). The number of cases treated is too small to judge the efficacy of sulfathiazole therapy. However, it is worth mentioning a few factors that influenced the course of these cases. Four of the patients (Cases 1, 4, 5 and 6) were forty years of age or older, and one of them recovered (Case 4). Of 40 patients over forty years of age, Skinner and Keefer⁴ observed that only 1 recovered. Mendell³ reports 1 recovery in 9 patients over forty years of age. Perhaps more important than the age of the patients treated is the accessibility of metastatic abscesses to surgical drainage. In the 3 patients who recovered (Cases 2, 4 and 7) the abscess was drained. In Case 4, there was, in addition to the abscess in the right thigh, an empyema that became sterile during sulfathiazole therapy. In the series of 22 patients who recovered that was studied by Skinner and Keefer,⁴ 21 had localized lesions that were incised and drained. It seems justifiable, then, to state that surgical drainage of the localized staphylococcal abscesses is essential to recovery in most cases.

With the exception of sterilization of the empyema cavity in Case 4, we have not observed an abscess that became sterile under treatment with sulfathiazole. What place, then, has the drug in the treatment of these infections? We have demonstrated that sulfathiazole when given by mouth to normal persons and to patients with bacteremia increases the bactericidal and bacteriostatic action of the blood against pathogenic staphylococci. In our experience sulfathiazole either sterilized the blood stream or lowered the number of organisms in the circulating blood. This

action may be valuable in the prevention of metastatic abscesses during the period of blood-stream invasion. It has been pointed out that 82 per cent of all cases with bacteremia develop secondary lesions, and it is the development of these metastatic abscesses which cannot be drained that determines the fatal outcome in the majority of cases.

To summarize, patients suspected of having a bacteremia due to *Staph. aureus* should have a blood culture done as soon as possible, following which sulfathiazole should be administered immediately. Daily blood cultures should be taken, and determinations of the concentration of sulfathiazole in the blood should be made. It is desirable to maintain a level of sulfathiazole in the blood stream of between 3 and 5 mg. per 100 cc.⁹ If the patient is anemic, blood transfusions should be given until the blood count is normal. The diagnosis and immediate drainage of all localized abscesses are of utmost importance. A sustained fever or blood cultures that continue to be positive are usually signs of further abscess formation, and a thorough search should be made for such lesions.

Treatment with sulfathiazole should not be undertaken without close observation for toxic manifestations. For this reason daily blood counts and urine analyses should be made. In the cases reported here no serious toxic manifestations were observed. Two patients (Cases 1 and 3) complained of nausea and occasionally vomited. One patient (Case 2) developed a mild anemia and on the eleventh day of treatment a generalized rash and fever were noted, which disappeared promptly following withdrawal of the drug. Case 7 showed injection of the conjunctivas and a lesion simulating erythema nodosum. No marked anemia or hematuria due to sulfathiazole was noted in these cases.

CONCLUSIONS

Seven cases of *Staphylococcus aureus* bacteremia were treated with sulfathiazole, and 3 recovered.

Following the administration of sulfathiazole in 3 cases, an increase in the bactericidal action of the blood against the invading organisms was demonstrated.

In normal persons the oral administration of sulfathiazole increases the bactericidal action of the blood against *Staph. aureus*.

Sulfathiazole usually sterilizes or decreases the number of organisms in the circulating blood, and therefore should be valuable in preventing the formation of metastatic abscesses.

The importance of blood transfusions and surgical drainage of localized abscesses is stressed.

78 East Concord Street

REFERENCES

1. Neubof, H., Aufses, A. H., and Hirschfeld, S. Pyogenic sepsis survey of one hundred and fifty cases. *Surg., Gynec. & Obst.* 58:886-896, 1934.
2. Bean, H. C. Clinical study of one hundred and nine cases of septicemia. *M. Sea Int.* 37:679-686, 1929.
3. Mendell, T. H. Staphylococcus septicemia: a review of thirty-five cases, with six recoveries, twenty-nine deaths and sixteen autopsies. *Arch. Int. Med.* 63:1068-1083, 1939.
4. Skinner, D., and Keeler, C. S.: unpublished data.
5. Foubinder, R. F., and Walter, L. A. Sulfanilamide derivatives of heterocyclic amines. *J. Am. Chem. Soc.* 61:2032, 1939.
6. Lawrence, C. A. Bacteriostatic actions of 3 thiazol derivatives of sulfanilamide upon bacteria in broth cultures. *Proc. Soc. Exper. Biol. & Med.* 43:92-97, 1940.
7. Long, P. H., and Bliss, E. A. Bacteriostatic effects of sulfathiazole upon various micro organisms: its therapeutic effects in experimental pneumococcal infections. *Proc. Soc. Exper. Biol. & Med.* 43:324-327, 1940.
8. Rammelkamp, C. H., and Stoneburner, L. T., III. Sulfathiazole: a clinical and in vitro study of its use in infections of the urinary tract. *New Eng. J. Med.* (in press).
9. Rammelkamp, C. H., and Keeler, C. S. Sulfathiazole effect on *Staphylococcus aureus* in vitro. *Proc. Soc. Exper. Biol. & Med.* 43:664-668, 1940.
10. Barlow, O. W., and Hom-Lurger, E. Specific chemotherapy of experimental staphylococcus infections with thiazol derivatives of sulfanilamide. *Proc. Soc. Exper. Biol. & Med.* 42:792-795, 1939.
11. Bliss, E. A., and Ott, E. Effect of sulfapyridine, sulfathiazole, and sulfamethylthiazole upon severe staphylococcal infection in mice. *Proc. Soc. Exper. Biol. & Med.* 43:706-709, 1940.
12. Herrell, W. E., and Brown, A. E. The clinical use of sulfamethylthiazole. *J. Am. Med. Ass.* 115:118-120, 1940.
13. Ca. W.
cases with apparent success report of animal experiments. *South M. J.* 33:83-87, 1940.
14. Weisman, D., and Russell, H. The treatment of acute staphylococcal infections with sulfamethylthiazole. *J. Pediat.* 17:31-37, 1940.
15. Stirling, W. C. Sulfathiazole: two cases of septicemia with recovery. *J. A. M. A.* 115:118-120, 1940.

TULAREMIA

Report of a Case Contracted on Cape Cod*

ROBERT E. MOSS, M.D.,† AND LLOYD R. EVANS, M.D.‡

BOSTON

TULAREMIA, specifically recognized, has been very rare in Massachusetts and the other New England states. In 1939, Badger¹ reported the second case diagnosed in this commonwealth—the fifth recorded in New England. Yet Cape Cod is infested with common wood ticks (*Dermacentor variabilis*), and in 1937 cottontail and jack rabbits imported from the West were released in this area both by state game conservation officers and by local sporting clubs. Badger's case, the first ever reported on the Cape, was contracted at West Falmouth in 1937.

Since that time, 2 additional cases of tularemia have been reported to the Massachusetts Department of Public Health,² 1 in 1938 and 1 in 1939. The latter chanced to come under our care as a routine hospital admission. Because of the conditions that favor the propagation of tularemia in the Cape Cod area, and the likelihood of disregarding the possibility of the disease in a specific case unless one's suspicion is aroused, we believed that this case should be reported.

CASE REPORT

C. G. N. (Medical No. 55,607), a 52-year-old widow, was admitted to the Medical Service of the Peter Bent Brigham Hospital on August 7, 1939, complaining of diarrhea and constipation, accompanied by fever, during the previous week.

The past history contributed nothing to an understanding of the illness, except that the patient had spent the

week prior to onset at a hotel in Falmouth on Cape Cod. She stated that the food had been bad and had made the help sick earlier in the summer.

She had been well, except for mild menopausal symptoms, until the evening of July 30, when she felt a "hot flash." This was accompanied by nausea, followed by vomiting. Thereafter she felt fairly well, although somewhat feverish. Later in the evening she again vomited material containing nothing resembling blood or coffee-grounds. She found her temperature to be 104°F., and called her physician, who confirmed the temperature reading. That night she slept poorly because of a feeling of warmth and an intense headache. Also, she "ached all over," as if she were "getting the grippe."

The next day she remained in bed, following a liquid diet prescribed by her physician. She had one watery bowel movement, the temperature fell to 103°F., and she felt "wishy-washy." Thereafter, she remained in bed up to the time of admission.

On August 1, she found a small flat bug on her nightgown, and noted a small, sore spot, resembling a mosquito bite, on the posterior surface of the left thigh. Again, she had one watery bowel movement. Then, a dry, hacking cough developed, which persisted, though diminishing in frequency, until admission. A "cold sore" appeared in the mouth at this time. The next day the headache was almost negligible, and the temperature was normal.

On August 3, she had no bowel movement. In the morning, she had "chills," and the temperature went to 101°F., where it remained for the next 3 days, with an afternoon rise to 102. On August 6, she felt well enough to take solid food, which was well tolerated. The next day, she was given a productive enema. Because the temperature was still 102°F., and because he was leaving the city, her physician referred her to the hospital for further study.

The patient had applied poultices of hot boric acid solution to the sore spot on the left thigh. The area had increased in size, however, and without forming a pustule had formed a central scab. Other treatment had

*From the Medical Clinic, Peter Bent Brigham Hospital.

†Assistant resident physician, Massachusetts Memorial Hospitals, formerly medical house officer, Peter Bent Brigham Hospital.

‡Voluntary graduate assistant, Peter Bent Brigham Hospital.

consisted of powders for diarrhea and vomiting, and aspirin while the headache persisted.

Physical examination showed a well-nourished and well-developed woman. She seemed very warm, tolerating only the lightest covering, and was moderately restless. No sign of the previous cold sore persisted about the mouth. The heart was slightly enlarged, but otherwise appeared normal. The blood pressure was 118/80. The lungs were normally resonant and without abnormal sounds. The abdomen was not distended or tender; no masses or organs could be felt. On the lower third of the posterior aspect of the left thigh was a red wheal 4 cm. in diameter, in the center of which was a black scab 1 cm. in width. A slightly enlarged, firm, nontender node was felt in the femoral triangle on the left. Examination was otherwise not noteworthy.

On admission the urine showed a slight trace of albumin, with a negative sediment. On the 3rd day there was a very slight trace of albumin with an occasional white blood cell in the sediment. Thereafter, examination of the urine was negative, except for a rare red blood cell in one specimen, and 10 or 12 white blood cells per high-power field in another.

The hemoglobin ranged from 95 to 105 per cent (Sahli). The red-cell count varied from 3,000,000 to 4,400,000. The white-cell count was 11,750 on admission, rose to 14,600 on the third day, fell to 8850 on the twelfth day, and was 10,950 when last taken a week before discharge. The differential count showed 72 per cent polymorphonuclears, 13 per cent large lymphocytes and 15 per cent small lymphocytes. Blood Wassermann and Hinton tests were negative. The corrected sedimentation rate on August 19 was 19 mm. in 10 minutes. Blood cultures were done daily for 12 days and were all negative. A Widal test on August 10 was negative in dilutions from 1:1 to 1:100. Agglutination tests against paratyphoid A and B bacilli were questionably positive in a 1:1 dilution, but negative in dilutions of 1:25 and 1:50.

The Bacteriological Laboratory of the Massachusetts Department of Public Health reported that blood taken on the 2nd day showed negative agglutination tests against typhoid and paratyphoid A and B bacilli, *Brucella abortus*, dysentery organisms and *Proteus* X19. On August 14 the same laboratory reported a positive Weil-Felix reaction in a dilution of 1:25. Beginning on the 2nd day, four blood specimens were sent to the National Institute of Health for agglutination tests. The results are shown in Table 1.

TABLE 1. Dilutions Giving Positive Agglutination Tests, as Reported by the National Institute of Health.

DATE SPECIMEN TAKEN	<i>Past. tularensis</i>	<i>Br. abortus</i>	<i>E. typhi</i>	<i>Proteus</i> X19	<i>Proteus</i> OX2
8-8-39	0	0	0	1:80	0
8-14-39	1:320	0	0	1:40	1:10
8-22-39	1:1280	1:80	1:10	1:40	1:20
8-30-39	1:1280	1:20	1:10	1:20	

Repeated stool cultures were negative, except for *Escherichia coli*. A brucellergin skin test was negative at 10 minutes, showed a +++ reaction at 24 hours and a + reaction at 48 hours. On August 31, a *Pasteurella tularensis* skin test, performed with material supplied by Dr. Lee Foshay, gave a 0.7-cm. wheal with a 5.0-cm. area of erythema at 48 hours. Blood injected into a male guinea pig on August 14 showed no evidence of Rocky Mountain spotted fever.

An x-ray film of the chest, taken with a portable machine, showed the lungs to be clear on August 9.

The temperature on admission was 102.4°F., with a pulse rate of 84 and respirations of 34. The temperature fell by lysis, reaching normal on the 15th day, but rose above 99°F. nearly every afternoon until discharge. The pulse tended to remain between 80 and 90, although the respirations usually ranged between 20 and 25. The bowels moved once or twice daily. At no time did the patient appear seriously ill.

Seven months after discharge the patient reported that she felt well. Her physician stated that the lymph node in the left groin had finally suppurred, requiring incision and drainage 3 weeks after discharge. Then the slight fever that had recurred while the lymph node was suppurating subsided permanently, despite the fact that the wound drained for about 3 months.

On admission, the most likely diagnosis was tularemia. This rare infection was suspected because of the excellent report by Badger,¹ in which he pointed out the presence of an almost ideal "tularemia set-up" on Cape Cod. The diagnoses that had to be ruled out were typhoid fever, Rocky Mountain spotted fever and tick-bite fever. Disparity between temperature and pulse rate and a story of having eaten bad food that allegedly had sickened others suggested typhoid fever, but it was rather easily ruled out by the repeatedly negative blood and stool cultures and Widal tests. Although we had no opportunity to see the insect found by the patient, we had to assume that it probably was a tick, and hence that she might have a tick-transmitted infection other than tularemia. The diagnosis was settled by the laboratory tests. The first reports of the agglutination tests from both the state and federal laboratories pointed toward spotted fever, despite the total lack of clinical evidence for this diagnosis. Table 1 shows that the agglutinin titer for *Proteus* X19 fell, whereas that for *Past. tularensis* rose strikingly. The guinea-pig test for Rocky Mountain spotted fever was negative. According to Badger,¹ Foshay reports frequent cross-agglutination of *Proteus* X19 in animals infected with tularemia, but rarely in man. Badger's case did not show a positive Weil-Felix reaction. Cross-agglutination of *Br. abortus* by tularemic serums has frequently been noted.³ Further proof of the correct diagnosis was obtained by means of the skin test with Dr. Foshay's preparation of *Past. tularensis*. This test was strongly positive according to his standards.⁴

Treatment of tularemia can be undertaken with a specific serum,⁴ or with sulfanilamide.⁵ Neither was considered vitally necessary, however, in this case, since the patient at no time appeared seriously ill. She was therefore given only bedrest and general care, and recovered, following the supuration of the left inguinal node, which was in-

cised three weeks after her discharge and which drained for three months. Whether serum therapy might have prevented this complication cannot be stated.

SUMMARY

A case of ulceroglandular tularemia, contracted on Cape Cod, is reported. The potentialities of

this tick-infested area as a source of future cases of tularemia are emphasized.

REFERENCES

- 1 Badger, T. L. Tularemia: report of a case of typhoidal form. *New Eng J Med* 220:187-191, 1939.
- 2 Massachusetts Department of Public Health personal communication.
- 3 Francis, E. A summary of present knowledge of tularemia. *Medicine* 7:411-432, 1928.
- 4 Foshay, L. Tularemia: a summary of certain aspects of the disease including methods for early diagnosis and the results of serum treatment in 600 patients. *Medicine* 19:183, 1940.
- 5 Curtis, W. L. Sulfanilamide in the treatment of tularemia. *J A M A* 113:294, 1939.

PNEUMOCOCCAL CROSS-INFECTIONS IN THE HOME AND HOSPITAL*

HENRY A. HOLLE, M.D.,† AND JESSE G. M. BULLOWA, M.D.‡

NEW YORK CITY

THE refinement of the immunologic classification of the pneumococci by Cooper and her co-workers has facilitated the epidemiological study of the transmission of the pneumonias. The pneumococci present no distinguishing microscopic appearance. Formerly it was widely believed that the pneumococci often found in the nose and throat of healthy persons had no connection with the transmission of the disease, and that they were transformed into pathogenic forces by some unknown conditions or factors. Accordingly, many physicians and hospital administrators thought that precautions against the spread of the pneumonias were unnecessary. So long as it was impossible to distinguish different phases of a pneumonia as due to separate infections, many cases of cross-infection among pneumonias were not recognized, and recrudescence of fever was usually regarded as an exacerbation of the original disease.

Familial infections have been followed and reported by a number of observers,¹⁻⁶ but the recording of additional cases is valuable because of current widespread beliefs and practices that ignore the opportunity for prophylaxis. The first patient stricken in a family is rarely segregated, and when sent to hospitals patients are rarely individualized by an aseptic nursing and staff technique such as that used in the best hospitals for patients with infectious disease.

Cross-infections occur both in the home and in the hospital ward. Pneumococcal pneumonia is an acute communicable disease. The following hitherto unreported cases are given as evidence of

contagious infection. Five examples of cross-infection among families in the home, with the cases later admitted to the Harlem Hospital, and four cases developing on the wards of the hospital are presented.

FAMILY INFECTIONS

S FAMILY

Case 1. A. S., 7-year-old boy.

- 12/19/38. Onset with cough and fever.
- 12/21/38. Admitted to hospital; lobar pneumonia in right lower lobe, confirmed by x-ray examination.
- 12/22/38. Type 2 pneumococcus recovered from sputum; also alpha hemolytic streptococcus.
- 12/28/38. Discharged.

Case 2. C. S., 5 year-old girl. Sister of A. S.

- 12/24/38. Onset with cough, fever, chest pain.
- 12/28/38. Admitted to hospital; clinical and x-ray findings of consolidation of left lower lobe; Type 2 pneumococcus recovered from sputum.

In the S family, Type 2 pneumococcus pneumonia occurred in a younger sister within 3 days after the first patient was hospitalized, and within 5 days of the onset of the first patient.

C FAMILY

Case 1. S. C., 9 year-old boy.

- 12/26/38. Onset with cough and fever.
- 12/29/38. Admitted to hospital; lobar pneumonia in right lower lobe.
- 12/30/38. Type 1 pneumococcus recovered from sputum.

Case 2. A. C., 38-year-old woman. Mother of S. C.

- 12/27/38. Onset with chills, fever, cough.
- 1/3/39. Admitted to hospital; signs of pneumonia in right lower lobe, confirmed by x ray films; Type 1 pneumococcus recovered from sputum and blood.

*From the Littauer Pneumonia Research Fund, and the Medical and Pediatric services, Harlem Hospital, New York City. These studies received financial support from the Metropolitan Life Insurance Company and from Mr. Bernard M. Baruch, Mr. Bernard M. Baruch, Jr., Miss Belle N. Baruch and Mrs. H. Robert Samitig.

†Passed assistant surgeon, United States Public Health Service.

‡Clinical professor of medicine, New York University College of Medicine; visiting physician, Harlem Hospital.

Case 3. L. C., 18-year-old girl. Sister of S. C.

12/29/38. Onset with pain in left chest, cough, chills, fever.

1/3/39. Admitted to hospital. Signs of consolidation in left lower lobe, confirmed by x-ray examination; Type 1 pneumococcus recovered from sputum and blood.

Case 4. C. C., 49-year-old man. Father of S. C.

12/30/38. Onset with chill, pain in left chest, fever, cough.

1/3/39. Admitted to hospital; signs of consolidation in left lower lobe, confirmed by x-ray studies.

1/4/39. Type 1 pneumococcus recovered from sputum.

Case 5. D. C., 6-year-old girl. Sister of S. C.

Date of onset unknown.

1/4/39. Admitted to hospital; diagnosis, lobar pneumonia.

1/7/39. Type 1 pneumococcus recovered from sputum.

Case 6. R. S., 3-year-old girl. Sister of S. C.

Date of onset unknown.

1/6/39. Admitted to hospital; diagnosis, lobar pneumonia; Type 1 pneumococcus and beta hemolytic streptococcus found in sputum.

The 7 members of the C family lived together in a small five-room apartment. S. C. (Case 1) slept with H. C., the only member of the family to escape infection with Type 1 pneumococcus. S. C. developed a cough with fever on December 26, 1938, and because he appeared so sick he slept with his mother, A. C. (Case 2), from December 26 to 29, at which time he was admitted to the hospital. A. C. developed chills, fever and a cough on December 27 and went to bed, but got up at intervals to administer to her sick family. She was finally admitted on January 3, 1939, with a bacteremia.

S. C. was taken to the hospital on December 29, 1938, by L. C. (Case 3), an older sister. It was necessary for L. C. to wait for some time before S. C. was admitted. As a result she missed her dinner and got very cold. While waiting she held S. C.'s head in her lap. That night she developed chills and slept with her mother, A. C., who was already ill. She was admitted with A. C. on January 3.

C. C. (Case 4) nursed his wife, A. C., and daughter, L. C., after working-hours until he became ill on December 30, 1938. He was admitted on January 3, 1939.

D. C. (Case 5) and R. S. (Case 6) slept in the same bed. The exact dates of the onset of their pneumonias are not known, but judging from the fact that the mother did not know of their illness until later, it is assumed that the onset occurred after the latter had left for the hospital on January 3. D. C. was admitted on January 4, and R. S. on January 6.

SU FAMILY

Case 1. E. S., 36-year-old man.

10/31/38. Onset with pain in right chest, cough, expectoration.

11/3/38. Admitted to hospital; signs of pneumonia in right lower lobe.

11/4/38. Type 5 pneumococcus recovered from sputum.

Case 2. E. S., Jr., 11-year-old boy. Son of E. S.

11/1/38. Onset with upper-abdominal pain.

11/5/38. Admitted to hospital; dullness in left lower lobe.

11/6/38. Type 5 pneumococcus recovered from pharyngeal aspirate; x-ray examination showed consolidation at left base.

Family Su is an instance of Type 5 pneumococcus pneumonia in a father followed 1 day later by a similar infection in the son.

P FAMILY

Case 1. R. P., 3-year-old boy.

12/25/38. Onset with cough and fever.

12/27/38. Admitted to hospital; signs of consolidation in left lower lobe, confirmed by x-ray film.

12/28/38. Type 5 pneumococcus recovered from sputum.

12/30/38. Types 5 and 14 pneumococci recovered from laryngeal evacuate.

Case 2. R. P., 3-year-old boy. Twin brother of R. P.

12/27/38. Admitted to hospital with upper-respiratory infection.

12/28/38. Temperature rose above 104°F.

12/29/38. Physical signs of pneumonia; no definite consolidation.

12/30/38. Type 5 pneumococcus recovered from pharyngeal aspirate.

The P family presents an interesting history of 2 brothers. R. P. (Case 1) became ill on December 25, 1938, with cough and fever. He was admitted on December 27 with a diagnosis of pneumonia, Type 5 pneumococcus. R. P. (Case 2) was admitted at the same time with upper-respiratory infection and developed a pneumonia due to Type 5 pneumococcus on the following day.

W FAMILY

Case 1. J. W., 9-year-old girl.

12/15/38. Onset with persistent cough.

12/20/38. Admitted to hospital; crepitant rales right and left lower lobes; x-ray findings, scattered patches of consolidation in mid-portion of right lung. Type 1 pneumococcus recovered from sputum.

Case 2. C. W., 30-year-old woman. Mother of J. W.

12/25/38. Visited daughter in hospital.

12/26/38. Onset with chills, fever, pain in chest, cough.

12/29/38. Admitted to hospital; clinical and findings consistent with pneumonia in right lower lobe.

12/30/38. Type 1 pneumococcus recovered from sputum.

12/31/38. Type 1 pneumococcus found in patient later developed arthritis left sternoclavicular joint, from which Type 1 pneumococcus was recovered.

C. W. (Case 2) slept with J. W. (Case 1) until the latter was admitted to the hospital.

Although the evidence that each of the infections described above was transferred from person to person within the several families is not in controvertible, the occurrence of infections with identical pneumococcal types can hardly be explained as coincidence. The fact that these cases were observed during only two months suggests that simultaneous or almost simultaneous infections with identical pneumococcal types within families, such as the C family, are not uncommon.

pneumonia in the left lower lobe due to Type 5 pneumococcus, for which she had received therapeutic serum on January 4. A T, who had been afebrile for 4 days, was seen at the patient's bedside and was immediately ordered back to bed. However, 2 days later the patient was seized with a severe pain in the right chest and had an elevation of temperature. Type 7 pneumococci were recovered from the sputum on the same day, and x-ray examination revealed an area of consolidation in the base of the right lung, which became more extensive on January 13.

CASE 2 G S, a 46-year-old man was admitted on July 2, 1937, and was found to have pneumonia of the left lower

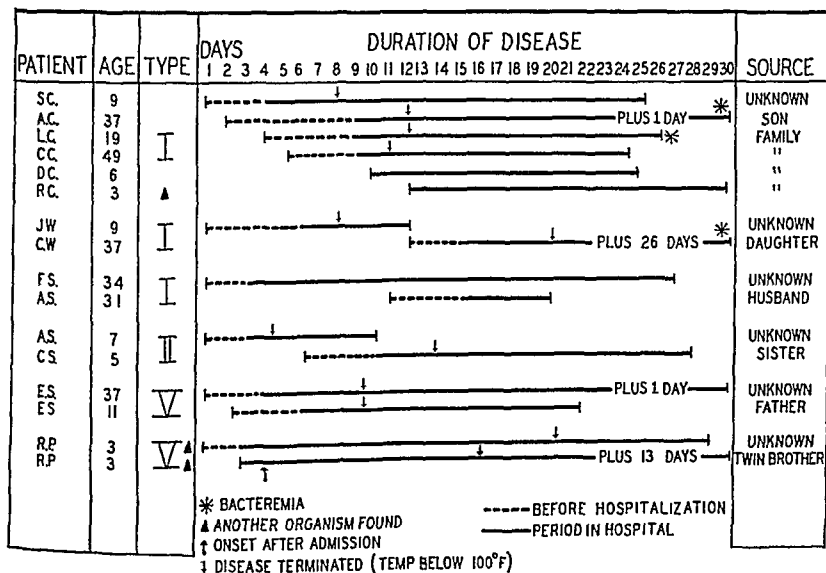


FIGURE 1 Family Infections

mon. There is reason to believe that if each patient admitted were carefully questioned regarding other illnesses in the family, many additional cases of cross infection would be discovered. Pneumonia prevention in the home seems to deserve more emphasis than has been placed on it in the past, and early isolation is probably an important factor. In addition, rapid active or passive immunization against specific types of the pneumococcus, with improved antigens or antiserums, and possibly chemoprophylaxis, offer themselves for study.

HOSPITAL-WARD INFECTIONS

CASE 1 B C, a 34-year-old woman, was admitted to the hospital on January 3, 1939, on the 2nd day of pneumonia in the left lower lobe due to Type 7 pneumococcus. She was visited on January 9 by A T, a 30-year-old woman, who was ambulant in the ward recuperating from

lobe due to Type 2 pneumococcus. From July 6 to 17 he occupied a bed adjacent to C S, who had pneumonia of the left lower lobe due to Type 4 pneumococcus. On July 20 the patient complained of pain in the right chest and began a new febrile course. The next day Type 4 pneumococcus was found in the sputum, and x-ray examination of the chest revealed consolidation in the right lower lobe.

CASE 3 Dr. H, an intern at the hospital, was admitted on October 11, 1938, with pneumonia of the right upper lobe. Type 20 and Wilder type pneumococci were recovered from the sputum, and he received appropriate treatment. During his illness a special nurse was assigned but on October 16 the nurse caring for C T, who was in an adjacent ward recovering from a Type 2 pneumonia of the right lower lobe, was assigned to the patient while still continuing to care for C T. The next day, the Wilder type pneumococcus was recovered from the sputum of C T, who did not, however, develop a new pneumonia involvement.

CASE 4. A man, suffering from Type 1 pneumococcus pneumonia, was treated on the 6th day of his illness with sulfapyridine and serum. He developed a pericarditis and a Type 1 pneumococcus empyema. The empyema was drained, and the temperature and pulse fell to normal. The temperature then rose to 103°F. and a purulent pericardial effusion from which *Streptococcus hemolyticus* grew was found. The patient was aspirated when there were signs of cardiac tamponade. He died the same day. Although the source of the hemolytic streptococcus could

— and Case 4 a disaster that followed secondary infection with *Str. hemolyticus*.

CONCLUSIONS

Pneumonia is a communicable disease. Patients suffering or convalescing from pneumonia due to a given type of pneumococcus may become infected by pneumococci of other types or

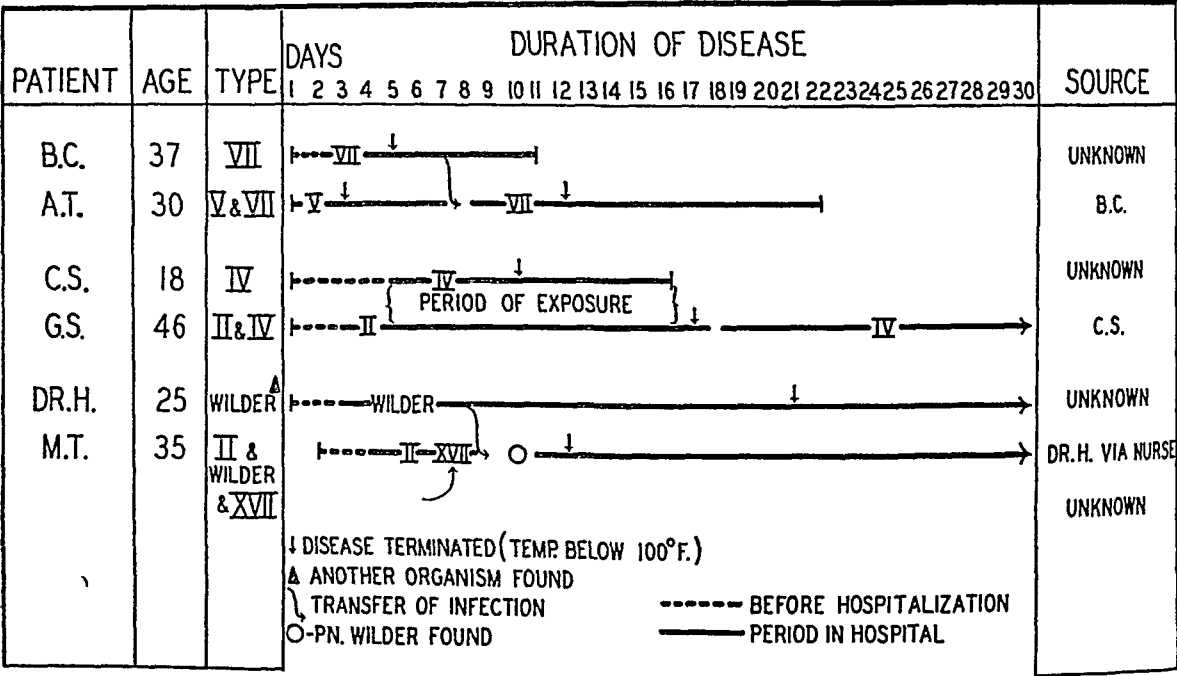


FIGURE 2. Hospital-Ward Infections.
The "Wilder" pneumococcus is now known as Type 33.

not be ascertained, the complication undoubtedly represented a cross-infection.

The first two of the cases just described were selected because they represent tandem infections in pneumonia patients, in which exacerbation of temperature and extension of the lesion would not have been correctly interpreted without the bacteriological studies that were undertaken. Previous bacteriological examination of the sputums and throat cultures failed to reveal the organisms which were found after exposure to known sources and which induced infection. Case 3 illustrates the possibility of spread by a vector,—the nurse,

by other organisms if an aseptic technic is not maintained.

REFERENCES

1. Tilghman, R. C., and Finland, M.: Pneumococcal infections in families. *J. Clin. Investigation* 15:493-499, 1936.
2. Finland, M., and Tilghman, R. C.: Bacteriological and immunological studies in families with pneumococcal infections: the development of type-specific antibodies in healthy contact carriers. *J. Clin. Investigation* 15:501-508, 1936.
3. Bullova, J. G. M.: *The Management of the Pneumonias: For physicians and medical students.* 508 pp. New York: Oxford University Press 1937.
4. Schroder, M. C., and Cooper, G.: An epidemic of colds, bronchitis and pneumonia due to type V pneumococci. *J. Infect. Dis.* 46:384-392, 1930.
5. Smillie, W. G.: A study of an outbreak of type II pneumococcus pneumonia in the Veterans Administration Hospital at Bedford, Massachusetts. *Am. J. Hyg.* 24:522-535, 1936.
6. Benjamin, J. E.; Rueggesser, J. M., and Senior, F. A.: Cross infection in pneumococcal pneumonia. *J. A. M. A.* 112:1127-1130, 1939.

HODGKIN'S DISEASE

Report of a Case with Unusual Longevity and Invasion of the Heart and Pericardium

MAX RITVO, MD *

BOSTON

THE purpose of this communication is to report a case of Hodgkin's disease that presented two unusual features. First, the patient survived a very long time, seventeen years having elapsed from the date when enlarged lymph nodes were first noted in the neck until death ensued. Secondly, at the post mortem examination it was found that the pericardium and the heart were involved; the process had extended directly through the cardiac wall, and a mass measuring 10 by 15 by 15 cm had projected into the lumen of the right auricle. In view of the rarity of invasion of the heart in Hodgkin's disease, it was deemed worthwhile to record this case.

CASE REPORT

The patient was a white, married woman. In 1920 when 32 years of age, she noticed a large swelling in the right side of the neck. She had borne two children and had had a subsequent miscarriage. The family and past histories were noncontributory. In July, 1922, she again became pregnant and the mass in the neck began to increase in size, a somewhat smaller but similar mass appeared on the left side. In November, 1922, 150 mg of radium screened with brass and 25 cm of wood was applied to the right supraclavicular region for 6 hours and to the left side for 2 hours. The enlarged lymph nodes diminished markedly but did not disappear entirely.

During the last 3 months of pregnancy, the cervical nodes increased greatly in size, and others appeared in the axillae and groins, the patient complained also of marked substernal pressure, dyspnea and a severe dry cough. The advisability of terminating the pregnancy was discussed, but the patient insisted on going to term, and was delivered of a normal baby girl in March, 1923. When she was seen the following month, large masses of lymph nodes were visible and palpable in both supraclavicular regions, the neck, the axillae and the groins. The spleen could be felt at the level of the iliac crest and extended across the midline. The liver was moderately enlarged. The right knee and leg were swollen, and there was severe pain radiating down both legs. The dyspnea, cough and substernal pressure had increased, and there was marked weakness. X ray studies of the chest revealed a dense, uniform mass 7 by 5 cm extending into the right mid chest from the root of the lung. X ray therapy was administered in April and May, 1923. Judged by modern standards, the dosage was small. Ten minute exposures were given, each consisting of 8 milliramp at 140 kv with 4 mm of aluminum filtration and a 40-cm target skin distance. The neck, chest, spleen and groins were irradiated each area receiving two exposures, treatments

were given at intervals of 2 or 3 days. The response was prompt, and the nodes soon disappeared almost completely. The spleen and liver were no longer palpable, and the pain, cough and dyspnea were relieved.

The patient was next seen in August, 1923, when examination showed a small swelling in the right side of the neck. No other nodes were found. The red cell count was 5,400,000 with 85 per cent hemoglobin and the white cell count 7300, with 65 per cent polymorphonuclears, 25 per cent lymphocytes, 9 per cent monocytes and 1 per cent eosinophils. The platelets were normal. The patient looked and felt well, the only complaints being a vague sense of weakness and a tendency to easy fatigability.

In June, 1925, there was a recurrence, with a node 2 cm in diameter in the right supraclavicular region and several smaller ones in the left side of the neck. X ray films showed a definite increase in size of the right hilar nodes. X ray therapy was given as previously, again with definite improvement. Neither a general nor a local unfavorable reaction followed the treatment. The patient's health and weight became excellent, and she was able to carry on all her usual duties as a housewife.

In January, 1927, and again in September and December of that year, four x ray treatments were given to the neck and right side of the chest because of local recurrences. There was slight nausea and loss of appetite, these ill effects were of short duration, and the response to x ray therapy was good. Thereafter the patient was observed at frequent intervals, but required no treatment until September, 1929, when the recurrence was slightly severer than previously. The node in the right neck measured 2 by 3 cm and was very firm. The mass in the right chest extended from the level of the second rib to that of the fifth rib anteriorly, and from the mediastinum to the midclavicular region. The trachea was deviated to the left. Response to x ray therapy was again good.

From 1930 to 1935, there were recurrences at intervals of several months, with a gradual lessening of the response to treatment. The voltage was 185 kv, with a 0.5 mm copper filter, 200 r being administered at each exposure. The patient's general condition remained good throughout this period. She was not confined to bed at any time and continued with her usual duties except that she required more rest.

In the latter part of 1935 and during 1936, the patient gradually failed. The nodes in the neck and mediastinum enlarged markedly, and there was increasing loss of weight together with dyspnea, cough, poor appetite and weakness. Hospitalization became necessary and she was admitted on November 10, 1936. X ray treatments of 200 r each were given daily (4 milliramp at 200 kv with a 40-cm distance and a filter of 1 mm of copper and 1 mm of aluminum, over a 10 by 10-cm field). At no time was an erythema produced. The entire chest and neck, however, assumed a deep tan, and several fine

*Assistant professor of roentgenology, Harvard Medical School, visiting physician, X ray Department, Boston City Hospital.

telangiectases appeared over the right side of the neck and chest. Symptomatic improvement resulted, and the nodes diminished somewhat. This improvement was of short duration, however, and in the spring of 1937 the patient became much worse. The weakness increased, and there were orthopnea, severe cough, hoarseness and loss of weight. The blood showed severe secondary anemia. In addition, gradually increasing cyanosis and congestion of the face, neck and upper extremities developed. Severe mental depression became a disturbing factor, with fits of

aorta were compressed backward but were not actually invaded by the tumor. The trachea appeared surrounded by the growth. No space was found between the visceral and parietal portions of the pericardium.

When the heart was opened, a tumor mass measuring 15 by 1.0 cm. was found extending through the cardiac wall and projecting into the lumen of the right auricle. The orifice of the superior vena cava was markedly compressed, barely admitting a small probe. The narrowed lumen of the vein continued through the tumor mass for

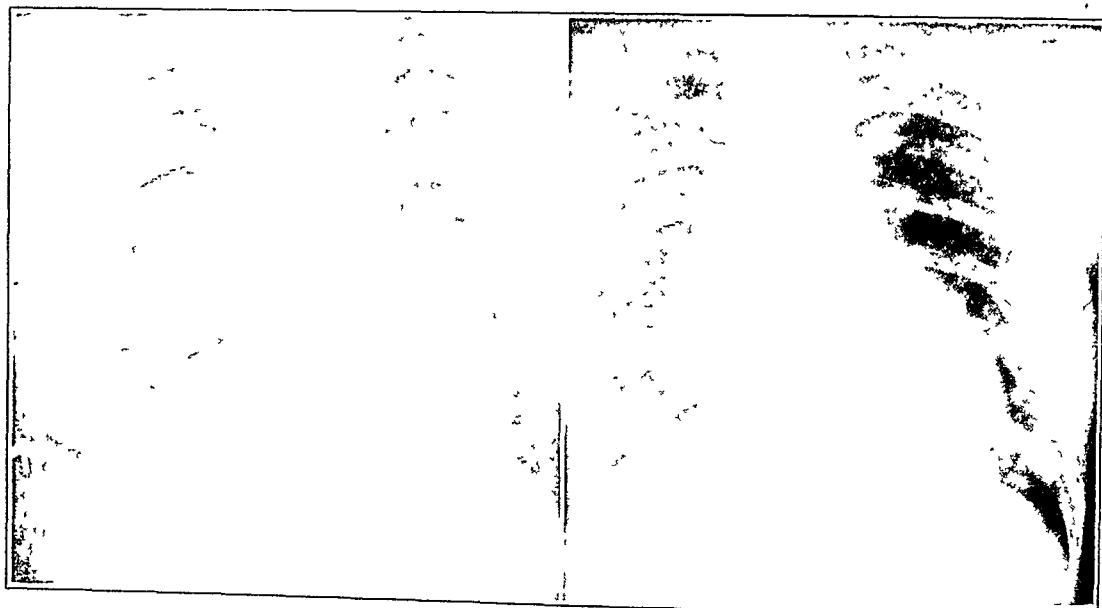


FIGURE 1. *Roentgen Films of the Chest Taken in 1927 (left) and 1930 (right). The mediastinal mass projects into the right mid-lung field.*

weeping and melancholia that were particularly striking because the patient had previously been active, happy and optimistic.

X-ray treatment, sedation and oxygen therapy were unavailing, and the patient died on June 14, 1937.

Autopsy. The body was that of an adult woman showing fair development and poor nourishment. Enlarged peripheral lymph nodes were present in the left axilla. There was no clubbing of the fingertips. The skin of the anterior aspect of the chest was purple and adhered to the underlying tissues, this change involving a triangular area with its apex at the suprasternal notch and the base about 7 cm. lower. The skin and underlying tissues were peeled from the chest with difficulty and contained a firm, infiltrating mass that measured 3 cm. in thickness. The first and second ribs on the left and the upper three ribs on the right were involved in the process and were of the same consistence as the tumor.

The superior portion of the anterior mediastinum was markedly thickened and adherent to the chest wall. The tumor above described extended directly from the mediastinum, and it was impossible to determine any line of demarcation between the chest wall, the right pleural cavity, the right lung and the mediastinum. On the left side, there were a few extensions of the growth between the pericardium and the left parietal pleura. The right pleural cavity contained 1100 cc. of greenish-yellow cloudy fluid, and in the left pleural cavity there was about 350 cc. of similar fluid.

The tumor extended into the neck, but exactly how far could not be determined. The esophagus and descending

a distance of about 6 cm. and then was completely occluded by the growth. The azygos system was dilated, and a fresh antemortem clot was present in one of the azygos veins. The left pulmonary artery was normal. The right pulmonary artery was markedly compressed at a point 4 cm. from the bifurcation, the lumen barely admitting a fingertip. The left common carotid and left subclavian arteries were displaced and encircled by neoplasm. The left innominate artery was also completely surrounded by tumor at its origin. The lumen of the right subclavian vein was narrowed, and the smaller branches of this vessel were thrombosed. The heart measurements were as follows: T.V. 11.5 cm., P.V. 8.0 cm., M.V. 8.0 cm., A.V. 10.3 cm., R.V. 1.4 cm. and L.V. 4.0 cm. The tumor ended at the heart border, except in the area where it entered the right auricle.

The mass in the chest in its entirety measured 15 by 15 cm. Serial sections revealed a dense, firm, white growth which did not pit and which cut with a gritty sensation. The left lung could be separated from the mass, but the medial border of the right lung could not be demarcated because the densely infiltrating growth involved the entire medial half.

The spleen weighed 140 gm. and was normal in shape. The gastrointestinal tract revealed no abnormalities. The liver weighed 1320 gm. and appeared normal in shape and consistence. The gall bladder, kidneys and adrenals were not remarkable.

Two of the sections of heart were taken from regions where the tumor had invaded the auricular musculature. These areas showed tumor masses projecting into the

auricle but not covered by endothelium. In places the tumor was extremely cellular, but in others it had undergone necrosis and fibrosis. The cellular areas were composed of an abundant stroma of fibrous tissue in which a variety of cells were present. There were many eosinophils and a number of monocytes with numerous large cells irregular in shape, containing vesicular nuclei and prominent dark nucleoli and many multinucleated giant cells. In a central portion of the tumor there was a small spicule of bone. The cells infiltrating the myocardium were similar in appearance to those making up the bulk of the tumor.

One section of lung revealed a large area of invasion by tumor, parts of which were converted into collagenous

tissue involving the mediastinum, lung, heart, pericardium, chest wall, axillary nodes and subcutaneous tissue. Postirradiation fibrosis, obstruction of the superior vena cava, thrombosis of the azygos vein, bilateral hydrothorax.

It is known that Hodgkin's disease may occasionally run a relatively benign and very prolonged course. Gilbert¹ cites cases that lasted twenty years and more. Jackson² reports a case in which the involved nodes were removed surgically with no recurrence after a lapse of twenty-six years, and another in which the patient sur-

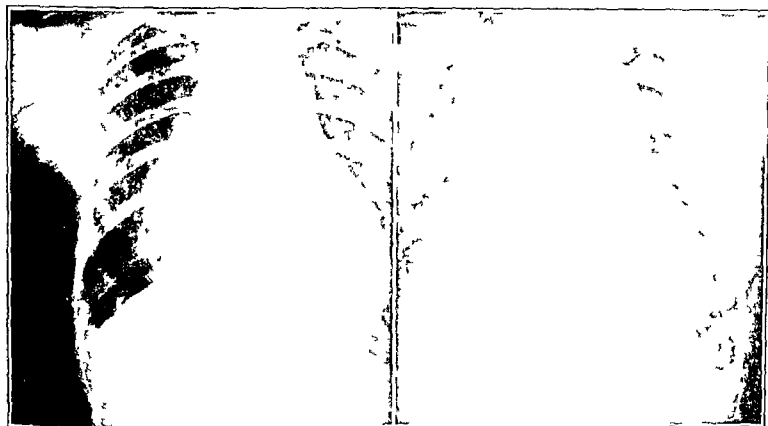


FIGURE 2 Roentgen Films of the Chest Taken in 1935 (left) and 1937 (right)
Note the marked increase in the size of the mass in the last film

tissue. Other regions were cellular and showed a picture similar to the tumor that had invaded the heart. At the transition between the tumor and lung, groups of cells were seen breaking through the alveoli and producing small patches of ulceration. The second section contained an extensive area that appeared to have been tumor but was undergoing degeneration and fibrosis. Most of the remaining portion of this section consisted of lung tissue, the markings of which had been obliterated by fibrin and scattered polymorphonuclear cells. The rest of the lung showed a moderate to marked edema with congestion of the capillaries.

Two sections taken from the mediastinal mass were studied. In one, degeneration and fibrosis had occurred to such a degree that a histological diagnosis was impossible. Essentially the picture was one of degeneration and fibrosis with moderate cellularity consisting chiefly of what appeared to be monocytes and irregular, undifferentiated cells. The second section of tumor contained striated muscle and large areas of tumor similar to those described in the previous section.

No tumor invasion was found in the liver. The firm demarcated area seen grossly in the spleen was found microscopically to consist chiefly of fibrosis.

The pathological diagnosis was as follows: Hodgkin's

disease. The patient survived for sixteen years. Although not unique in respect to longevity, the case here reported is extremely rare.

The prognosis in Hodgkin's disease is poor, the average period of survival being only two and a half to three years. Jackson³ recently reviewed this subject and summarizes the present knowledge as follows:

In Hodgkin's disease we find the most interesting data as to prognosis. The average duration of life from the first symptom in Hodgkin's lymphoma is two and a half years; yet nearly 50 per cent survive five years or longer, and nearly 20 per cent ten years or longer. In contrast, the average case of Hodgkin's granuloma lasts but a scant two and a half years and very few patients survive for over ten years; nearly three quarters are dead within three years. No person with Hodgkin's sarcoma has in our experience survived a three year period.

As the case here recorded is a Hodgkin's granuloma, the duration of life in the light of Jackson's statement is distinctly unusual.

It is generally agreed that in most cases treatment prolongs life for only a short while. The chief benefits resulting from therapy, particularly with the x-ray, are temporary shrinkage or complete disappearance of the involved nodes and the enlarged spleen, with consequent relief of pressure and the amelioration of other distressing symptoms. In consequence, the patient is often restored to good health for relatively long periods and is usually enabled to carry on practically all normal activities during these intervals. Occasionally a patient with an extensive and apparently

"lymphadenoma" in which the liver, lung and heart, as well as the lymphatic system, were involved. Gowers⁶ in a comprehensive study 1879 indicated that the pericardium and heart muscle could be involved in this condition. In spite of these early reports, many of the modern texts and treatises on Hodgkin's disease either make no reference to the possibility of cardiac invasion or note it only very briefly. Longcope⁷ states that although there may be cardiac displacement from the mediastinal masses, the heart itself is not involved in the disease. Ewing⁸ mentions that

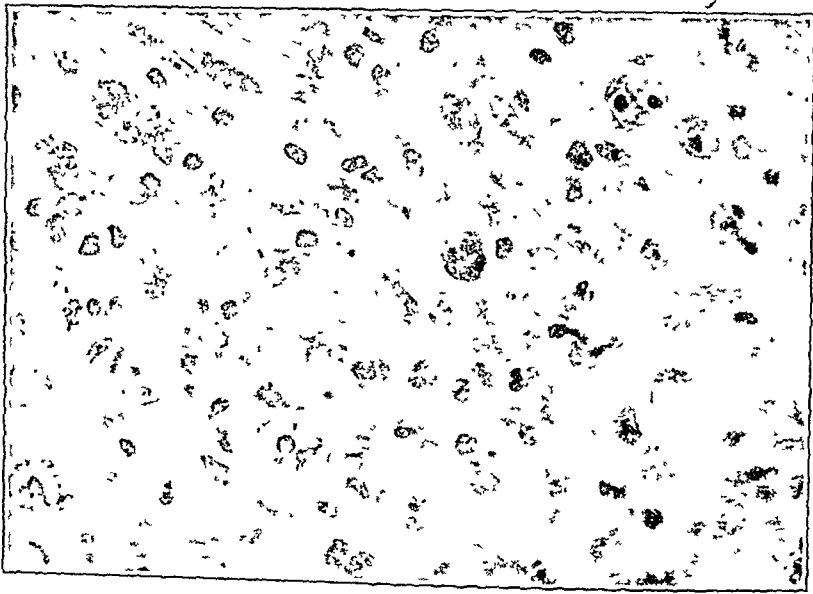


FIGURE 3. Photograph of a Section through the Central Portion of the Tumor.

severe form of the disease lives in comparative comfort for a long time, as in the present case. It is impossible to determine in advance, either on the basis of clinical experience or by any known test, which case will progress favorably and which will fail to respond to therapy. Therefore, every patient with Hodgkin's disease should be given the full benefit of early, thorough and persistent x-ray therapy.

In Hodgkin's disease, the involvement is primarily in the lymphoid structures, although infiltrations may occur in practically every tissue and no part of the body appears to be entirely immune. However, cardiac and pericardial lesions are very rare, and these organs are among the least commonly involved.

Hodgkin,⁴ in his first observations of the condition which now bears his name, noted that the disease was not confined to the lymphoid tissues alone, and in 1869 Murchison⁵ cited a case of

tensions to the heart have been noted. A few scattered references are found in the recent literature. Yates and Bunting⁹ described a case that involved the visceral pericardium. McAlpin¹⁰ in a review of the Presbyterian Hospital (New York City) records found myocardial nodules in 2 cases: involvement of the pericardium in 1, and a lesion of the pericardium in 1. In the "Case Record of the Massachusetts General Hospital,"¹¹ a case of Hodgkin's disease involving the pericardium is cited. Harrell¹² reports an unusually interesting case in which he found a dense zone of Hodgkin's tissue extending into the pericardium, epicardium and myocardium. He also reviews 8 cases that he collected from the literature; of these, there was 1 with small masses in the epicardium, the remainder revealing involvement of the pericardium.

Invasion of the heart and pericardium in Hodgkin's disease is therefore a very rare occurrence.

as evidenced by the small number of cases recorded in the literature. The reasons for this are not clear. The relatively small amount of lymphoid tissue in the heart is doubtless an important factor. Harrell¹² believes that pericardial involvement may take place by retrograde extension through the lymphatics or by way of the blood.

The lesions in Hodgkin's disease may undergo

involvement of the pericardium and direct invasion of the heart by a mass projecting into the right auricular cavity

In the case herein recorded, the prognosis appeared grave early in the disease because of the severe condition and the extensive involvement. Yet under x-ray therapy the patient survived an unusually long time, was well for long periods, and did not suffer greatly until near the end. Hence,

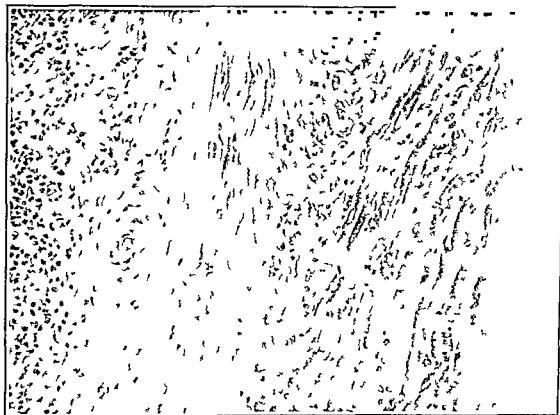


FIGURE 4 Photograph of a Section Showing Invasion of the Heart Muscle

a malignant degeneration, with the formation of a sarcoma. In the case herein recorded, however, there was no sarcomatous metamorphosis, the pericardial and cardiac involvement being by a granulomatous Hodgkin's lesion. No definite clinical or x-ray indication that the heart had been invaded was present during the patient's illness, the diagnosis being made post mortem. Since cardiac invasion is necessarily of the gravest prognostic import, it is of great interest to the clinician, roentgenologist and pathologist. If this possibility is borne in mind, the diagnosis can be correctly made—in some cases, at least—on the basis of the clinical and x-ray evidence.

SUMMARY

A case of Hodgkin's disease presenting two very striking features is reported. First, the duration of the disease was seventeen years, an unusual longevity. Secondly, the patient at autopsy showed in

early, persistent and thorough x-ray therapy is indicated in every case.

485 Commonwealth Avenue

REFERENCES

- 1 Gilbert R, Babatz L and Kadanka S. L influence de la roentgenotherapie sur l'evolution de la granulomateuse maligne. *Acta radiol* 15:508-512 1934
- 2 Jackson H Jr. Notes on treatment and prognosis of Hodgkin's disease and allied disorders. *W Clin North America* 21:361-368 1937
- 3 Lefevre J. Hodgkin's disease and allied disorders. *New Eng J Med* 220:26-30 1939
- 4 Hodgkin T. On some morbid appearances of the abscent glands and spleen. *Tr Med Chir Soc London* 17:68-114 1832
- 5 Murchison T. Case of a new morbid growth composed of nuclear tissue in the intestine liver kidneys lymphatic glands heart and other organs. *Tr Path Soc London* 20:192-196 1869
- 6 Gowers W R. Hodgkin's disease. *Reynolds's System of Medicine* Vol 5 1070 pp. London MacMillan & Co 18 9. Pp 306-352
- 7 Longcope W T. Hodgkin's disease. *Oster's Modern Medicine* Vol 5 948 pp. Philadelphia J Lea & Febiger 1927. Pp 226-259
- 8 Ewing J. *Neoplastic Diseases A treatise on tumors* Second edition. 1044 pp. Philadelphia W B Saunders Co 1971. P 3-0
- 9 Yates J L and Bunting C H. Rational treatment of Hodgkin's disease. *J A M A* 64:1953-1961 1915
- 10 McAlpin J R. Hodgkin's disease. *Nelson New Loose Leaf Medicine* Vol 3 625 pp. New York Thomas Nelson & Sons 1937. Pp 347-359
- 11 Case records of the Massachusetts General Hospital. Case 24791. *New Eng J Med* 219:99-101 1938
- 12 Harrell C T. Hodgkin's disease with invasion of pericardium and gallbladder: review of literature and report of case with autopsy. *Arch Path* 28:58-64 1939

MASSACHUSETTS MEDICAL SOCIETY PRIZE ESSAY

MULTIPLE PULMONARY THROMBI ASSOCIATED WITH
CYANOSIS AND RIGHT-SIDED CARDIAC HYPERTROPHY*

REPORT OF A CASE

VICTOR G. BALBONI, M.D.†

BOSTON

IN 1901 Abel Ayerza, then professor of medicine at the National University of Argentina, described in an unpublished lecture a condition termed "*cardiacos negros*." This syndrome was characterized by cyanosis, dyspnea, polycythemia, right-sided cardiac hypertrophy and eventually death in cardiac failure.¹ Clubbing of the fingers, cephalalgia, vertigo, somnolence and occasionally hemoptysis have since become well-recognized components of this syndrome. Twelve years later Ayerza's pupil, Arrillaga,² correlated the clinical picture with the pathological finding of arteriosclerosis of the pulmonary vessels. This he believed was the end result of chronic pulmonary diseases such as asthma, chronic bronchitis, tuberculosis, or pleural adhesions, all of which produced pulmonary emphysema. With the demonstration of syphilis of the pulmonary arteries by Warthin³ and Escudero,⁴ Arrillaga later came to consider syphilis the chief cause of pulmonary arteriosclerosis and its syndrome of *cardiacos negros*. Although many authors^{1, 5-9} are in agreement concerning the syphilitic etiology of pulmonary arteriosclerosis, it is now generally believed that syphilis is responsible for relatively few of these cases.¹⁰⁻¹²

Posselt¹³ in 1909 and later others^{11, 14, 15} have classified pulmonary arteriosclerosis into primary and secondary forms, according to whether the sclerosis developed from disease primary in the vessels themselves or was secondary to some other factor producing elevation of pulmonary pressure.

As so classified, primary pulmonary arteriosclerosis can be produced by syphilis of the pulmonary arteries, although this is probably a less frequent cause than it was previously supposed to be.^{10, 11} Extensive diminution in the size of the lumens of the pulmonary vessels has also been reported following influenza, rheumatic fever, certain allergic diseases and schistosomiasis of the pulmonary arteries.^{11, 16-20} In most cases the etiology

is obscure. In all the above-mentioned conditions, the process is thought to be an endarteritis obliterans affecting chiefly the small arterioles.^{10, 11, 21}

Secondary sclerosis of the pulmonary arteries, the commoner type. In this form, the process is thought to be an atherosclerosis of the large arteries resulting from conditions producing an elevated pulmonary arterial pressure such as chronic asthma, tuberculosis, pulmonary fibrosis, carcinoma of the lung, pleural adhesions, mitral heart disease, patent septal defects in the heart, patent ductus arteriosus and, last and probably least, frequently multiple pulmonary emboli.^{11, 14, 15, 22} However, in an exhaustive study of the pulmonary and vascular changes in mitral stenosis Parker and Weiss²⁴ have shown not only that the large vessels are affected, but also that the small arteries show intimal thickening, and that this may go on to vascular occlusion. These changes, though rarely sufficient to produce a complete Ayerza's syndrome, undoubtedly play an important role in the degree of cyanosis accompanying mitral stenosis.

Thus we see that there is no one cause of the Ayerza's syndrome. The following case is significant because the literature contains, in so far as I know, only four reports²⁵⁻²⁸ of the syndrome following multiple thromboses of the smaller pulmonary vessels without marked arteriosclerosis or arteriolar sclerosis.

CASE REPORT

A 66-year-old Greek laborer entered the Peter Bent Brigham Hospital on January 28, 1939, because of dyspnea, cyanosis of the face and swelling of the face and legs of 3 weeks' duration. The family history was noncontributory. The patient had been well and strong all his life. There was no history of heart or lung disease other than influenza 21 years before entry. Two previous hospital admissions, both in 1932, were for a bilateral herniorrhaphy and the treatment of hypertrophic arthritis. Six years previous to admission the patient entered the Out-Door Department complaining of puffiness under the eyes. The blood pressure at that time was 140/80, and the basal metabolic rate +5 per cent. Three years before hospitalization he first noted some dyspnea on exertion. However, this was not troublesome until 20 months before death, when he again came to the Out-Door Department, this time complaining of marked swelling of the legs. The heart was found to be moderately enlarged to the left, the neck veins were distended, and there was marked pitting

*Last spring the Massachusetts Medical Society offered a prize of fifty dollars for the best-written and most comprehensive case report submitted by an intern in any Massachusetts hospital approved by the American Medical Association for intern training. The competition closed on May 5. Six case reports were submitted, and a committee, consisting of the president of the Boston Medical Library, the editor of the *New England Journal of Medicine*, and the chairman of the Committee on Medical Education and Medical Diplomas of the Massachusetts Medical Society, served as judges. The prize was awarded to Dr. Victor G. Balboni.

†Formerly, intern in pathology, Peter Bent Brigham Hospital; medical house officer, Massachusetts General Hospital.

edema of the legs and lower abdominal wall. No cardiac murmurs were heard, the rhythm was regular, and the blood pressure was 130/90. On digitals and a low salt and high vitamin diet the edema disappeared and the heart appeared to decrease in size. For the next year the patient felt well except for slight substernal distress on exertion. Three weeks before admission he came to the Out Door Department complaining of cyanosis of the face and edema of his face and legs. In spite of bedrest these symptoms gradually increased, and on entry he was found to be quite ill and somnolent, though alert when aroused. The face, hands and feet were cyanotic in both the recumbent and the sitting position. The neck veins were found to be moderately distended, and the heart extended 11.5 cm to the left of the midsternal line and 5.0 cm to the right. The cardiac rate was 106, the rhythm was regular, no murmurs were heard, and the blood pressure was 135/80. Respirations were 28 and not labored. Coarse, moist rales and rhonchi were heard throughout

Oxygen given by intranasal catheter failed to relieve the cyanosis appreciably, and in spite of digitalis and supportive treatment the patient continued to fail. During the last 5 days of life the pulse was weak and extremely variable, showing extrasystoles and paroxysms of tachycardia. He became more and more cyanotic, the respirations became shallower, and death occurred on the 14th hospital day. A diagnosis of Ayerza's syndrome was made before death on the basis of cyanosis, polycythemia, cardiac hypertrophy with marked enlargement of the right side, slight clubbing of the fingers and somnolence. The low oxygen saturation of the blood, in the absence of a congenital defect in the heart producing a right-to-left shunt, and the failure to respond to oxygen were proof of a block between the alveolar air and the pulmonary circulation. The spinal fluid findings suggested a subarachnoid hemorrhage.

Autopsy A post mortem examination was made 14 hours after death. The body was that of a markedly cyanotic, well developed and moderately well nourished man and showed a moderate amount of pitting edema of the ankles, extending superiorly to the midportion of the tibiae. There was slight clubbing of the fingers, and in each inguinal region there was a well healed herniorrhaphy scar.

The liver and spleen showed passive congestion but were otherwise not remarkable. The prostate, which was rubbery and firm in consistence, showed moderate symmetrical enlargement. The aorta and tributaries showed a minimal amount of arteriosclerosis, and their elasticity was well preserved.

The heart weighed 530 gm. The pericardium was adherent to the anterior surface of the right ventricle by several fibrous adhesions. Beneath these adhesions there was a small area of calcification in the epicardium of the right ventricle 1.5 cm below the coronary sulcus, measuring 1.5 x 1.0 cm and less than 1 mm in thickness. As studied in situ the heart was enlarged both to the left and to the right, although the enlargement on the right side was by far the more striking. The right ventricular myocardium measured 15 mm in thickness, the left ventricular myocardium 23 mm. Except for the cardiac hypertrophy, both gross and microscopic examinations of the heart were essentially negative. No ante mortem thrombi were present in the ventricles, atria or their appendages, and the coronary vessels showed no appreciable atheromatous change.

Gross examination of the kidneys revealed several small, wedge-shaped areas of cortical infarction, each measuring 3 mm in width. Microscopically in these infarcted areas several moderately large arteries were found that were occluded by fibrinous thrombi exhibiting early peripheral organization. No noteworthy degree of arteriosclerotic changes was present in the vessels throughout the renal parenchyma and except for the small infarcts, the kidneys were essentially normal.

The brain weighed 1470 gm, was symmetrical and revealed no blood on or beneath the dura mater or pial arachnoid. Both occipital lobes were soft to palpation and their convolutions slightly flattened. This softening extended anteriorly from the occipital poles for approximately 5 cm and laterally from the longitudinal fissure on each side for 5 cm. Coronal sections revealed the softening on the right to be roughly spherical measuring 5 cm in diameter and involving the entire tip of the occipital lobe except for its inferolateral border. It extended anteriorly to the level of the sylvian fissure in the inferomedial aspect of the occipital lobe. On the left, the softening involved the entire white matter of the occipital lobe for a distance of 4 cm. The ventricles were symmetrical free



FIGURE 1 Organized Thrombus in Process of Canalization
Section taken from right upper lobe and stained with
eosin and methylene blue ($\times 275$)

both lung fields. The fingers were slightly clubbed. Vision in both eyes was limited to the differentiation of light and dark. The deep reflexes were not remarkable, and the pupils reacted poorly to light.

The laboratory findings were as follows. The red-cell count was 6,500,000, the white-cell count 17,500 and the hematocrit reading 61.5 per cent. The total protein was 4.5 gm per 100 cc and the nonprotein nitrogen 54 mg. The urine showed a specific gravity of 1.022, with no red blood cells, rare white blood cells and an occasional hyaline cast. The right antebraclial venous pressure was 203 mm of water, and the right femoral venous pressure 167 mm. The femoral arterial blood was 65.6 per cent saturated with oxygen, and the femoral venous blood was 93.7 per cent saturated. Electrocardiographs revealed no preponderance of either ventricle. A blood Hinton test was negative. The spinal fluid was under an initial pressure of 270 mm of water and contained 270 red blood cells per cubic millimeter.

from hemorrhage and not distorted. Microscopically, in the substance of both occipital lobes occasional small arteries were found to be occluded by fibrinous thrombi. The Virchow-Robin spaces were dilated and engorged with red cells, and the brain substance surrounding these vessels showed marked destruction and infiltration by polymorphonuclear leukocytes and mononuclear phagocytes. The remainder of the brain was not remarkable except for a moderate degree of intimal thickening of the arteries.

The right lung weighed 1140 gm., the left 420 gm. The



FIGURE 2. *Organized and Canalized Artery.*

Section taken from right upper lobe and stained with eosin and methylene blue ($\times 90$).

right superior lobe was bound firmly to the posterior and lateral parietal pleura by dense fibrous adhesions. Both the superior and inferior lobes on the left were adherent to the mediastinum, and the superior lobe was also adherent at its apex and along its posterior and lateral aspects to the parietal pleura. The superior lobes on the right and left were gray and crepitant to palpation; the inferior lobes were reddish gray and revealed little crepitus. There was an area of consolidation measuring 5 by 6 cm. on the anterior surface of the right inferior lobe that was found to be a well-encapsulated abscess. Much sanguinous fluid exuded from the cut surface of both lungs, but no grossly purulent fluid except from the previously mentioned abscess. No other areas of consolidation were noted. The pulmonary arteries were opened to their third ramification, and no thrombi were found. Occasional yellow plaques, none of which were ulcerated or calcified, were noted in these vessels. On close examination of the cut surfaces of the lungs many small vessels, measuring 2 mm. and less in diameter, were found to be occluded by dark-red thrombi. The bronchi contained considerable serosanguinous fluid. For microscopic study sections were made from thirty blocks of lung tissue taken from all portions of the lungs and stained with eosin and methylene blue, by Weigert's elastic-tissue method, with hematoxylin and eosin and with aniline blue. A considerable increase of fibrous tissue was noted about the bronchi and blood vessels and in the alveolar walls. The most marked pathologic changes were found in the small arteries of the lungs and in the alveolar walls supplied by these vessels. Throughout all lobes many of the arteries varying from 0.1 mm. to 2.0 mm. in diameter were occluded by thrombi. These were of various ages, some being completely organized and canalized (Figs. 1, 2 and 3), while into others only a few fibroblasts had extended from the vessel wall (Fig. 4). The most recently

formed thrombi were found in the vessels measuring 0.2 to 0.4 mm. in diameter. Frequently the thrombi appeared to be propagating in a retrograde manner into the larger vessels (Fig. 5). It was interesting that no thrombi were noted in the vessels measuring 0.09 mm. and less in diameter. These smaller vessels did show, however, concentric thickening of their walls such as is commonly seen in the kidneys in hypertensive disease. Splitting of the internal elastic lamina and intimal thickening were not pronounced in the thrombosed vessels, being no commoner than is customary in a person of corresponding age. There was no leukocytic infiltration of the vessel walls. In a patchy distribution throughout all lobes, and corresponding roughly to the distribution of the thrombosed arteries, there were groups of alveoli that showed considerable fibrous thickening of their walls. These thickened walls were practically avascular, and occasionally the lining epithelium had undergone metaplasia, becoming low cuboidal in type. In the lower lobes many of the more normal alveoli showed marked capillary engorgement and pericapillary edema



FIGURE 3. *Organized and Canalized Artery.*

Section taken from left upper lobe and stained with hematoxylin and eosin ($\times 85$).

Occasional alveoli contained a few "heart-failure" cells. There were also several true infarcts, only one of which was macroscopic in size; this had broken down, forming the previously mentioned abscess. The lower lobes bilaterally revealed a mild degree of bronchopneumonia, which was most marked in the right lower lobe.

A satisfactory pathogenesis of the predominating lesion, namely, a propagating thrombosis with organization and canalization of the pulmonary vessels, is not apparent. That these lesions were on a nonspecific infectious basis cannot be definitely excluded because of the peribronchial fibrosis. There was, however, no history of chronic bronchitis. Although Moller²² believes that it is possible to differentiate histologically autochthonous thrombi from emboli, an attempt to make such a distinction in this case forces one to agree with Brenner¹¹ that this is quite impossible. Arteriosclerotic changes in the pulmonary vessels were no

more extensive than was compatible with the patient's age, and there was no evidence of arteritis or endarteritis obliterans. No sources from which emboli could have arisen were found in the body, although it must be emphasized that the arms and legs were not dissected. There was no clinical evidence of thrombi in these regions.

The hypothesis entertained in this case is that spontaneous thromboses occurred in the small ves-

els throughout the lungs. After the formation of the thrombi the sequence of events leading to the morphologic changes in the lungs is more readily understandable. Following pulmonary-artery thromboses usually one of the following phenomena occurs. Either the lung tissue involved breaks down and is eventually replaced by scar tissue, or, if the pulmonary venous pressure is not appreciably increased, a small collateral circulation, probably from the bronchial arteries, maintains the alveolar walls intact. However, under the latter circumstances the alveolar walls are relatively avascular, and rapidly develop a marked increase of collagenous fibrous tissue, which separates the capillaries from the alveolar basement membrane. This fibrous thickening of the alveolar walls prevents free exchange of gases between the alveoli and their capillaries, and the functionless respiratory epithelium of the alveoli becomes low cuboidal in type.

As the above-described lesions spread through

the lungs in question, the pulmonary vascular bed was reduced. Pulmonary arterial hypertension, right-sided cardiac hypertrophy and eventually cardiac failure followed in the order stated. With cardiac failure the capillaries, especially those in the lower lobes, became engorged, and pericapillary and alveolar edema occurred. All three of these factors hinder the free exchange of gases in the remaining normal alveoli. Thus, the marked reduction in oxygen saturation of the arterial blood is the expected physiologic concomitant of the described morphologic changes in the lungs, that is, arterial occlusions with marked reduction in the pulmonary vascular bed, fibrosis of the alveolar walls, capillary engorgement and pericapillary and alveolar edema.

SUMMARY

A case of marked cyanosis, right-sided cardiac hypertrophy and cardiac failure in a man with-



FIGURE 4. *Thrombosed Vessel Showing Organization.*
Section taken from right lower lobe and stained with eosin and methylene blue ($\times 155$).

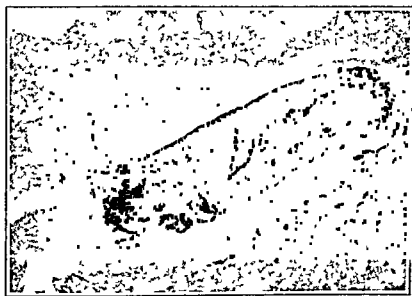


FIGURE 5. *Fresh Thrombus in Moderately Large Vessel.*
Section taken from left lower lobe and stained with hematoxylin and eosin ($\times 50$).

out known pre-existing heart disease is presented. Because of the markedly reduced oxygen saturation of the arterial blood in the absence of evidence of a right-to-left-sided vascular shunt in the heart, and the failure of the cyanosis to respond to intranasal oxygen, a block between the alveolar air and the pulmonary vascular bed was postulated. Autopsy showed this to be due to apparently spontaneous multiple thromboses of the smaller pulmonary vessels. Similar thrombi were found in both the brain and kidneys.

Various pathologic conditions that can produce Ayerza's syndrome are enumerated.

REFERENCES

- Konstam, G. L. S., and Turnbull, H. M.: Syphilis of lung with pulmonary arteritis (Ayerza's disease). *Lancet* 2:756-761, 1929.
- Arrillaga, F. C.: Esclerosis secundaria de la arteria pulmonar y su cuadro clinico (cardiacos negros). 261 pp. Buenos Aires Tesis, No. 2536, 1912.
- Warthin, A. S.: Syphilis of the pulmonary artery syphilitic aneurysm of the left upper division demonstration of the *Spirochaeta pallida* in the wall of the artery and the aneurysmal sac. *Am. J. Syph.* 1:693-711, 1917.
- Escudero, P.: Les cardiaques noirs et la maladie de Ayerza. *Arch. d. mal. du coeur* 19:439-445, 1926.
- Idem: Enfermedad de Ayerza. *Rev. de la Soc. de Med. Int.* 1:701-820, 1925.
- Arrillaga, F. C.: Esclerosis de la arteria pulmonar. *Semana méd.* 31:60-62, 1924.
- Hare, D. C., and Ross, J. M.: Syphilitic disease of pulmonary arteries: with account of case. *Lancet* 2:806-812, 1929.
- Achard, C.: Cardiaques noirs et artérites pulmonaires. *Bull. méd., Paris* 44:409-413, 1930.
- Caussade, G., and Tardieu, A.: Un cas d'artérite syphilitique du poumon (cardiaque noir). considerations sur la bronchite chronique syphilitique et la syphilis artérielle du poumon. *Arch. méd-chir. de l'app. respir.* 3:269-282, 1928.
- MacCallum, W. G.: Obliterative pulmonary arteriosclerosis. *Bull. Johns Hopkins Hosp.* 49:37-48, 1931.
- Brenner, O.: Pathology of vessels of the pulmonary circulation. *Arch. Int. Med.* 56:211-237, 457-497, 724-752, 976-1014, 1189-1241, 1935.
- Cheney, G.: Ayerza's disease. report of two cases. *Am. J. M. Sc.* 174:34-45, 1927.
- Posselt, A.: Die Erkrankungen der Lungenschlagader. *Ergebn. d. allg. Path. u. path. Anat.* 13:298-526, 1909.
- Yater, W. M., and Konstam, G. R.: Pulmonary arteriosclerosis. *M. Clin. North America* 12:1689-1700, 1929.
- Pund, E. R., and Phinizz, T. B.: Primary sclerosis of pulmonary artery. *Ant. Int. Med.* 5:1391-1396, 1932.
- Bacon, C. M., and Apfelbach, C. W.: Primary sclerosis of the pulmonary artery and its branches. *Arch. Path. & Lab. Med.* 3:801-815, 1927.
- Idem: Primary sclerosis of the pulmonary artery and its branches. *Tr. Chicago Path. Soc.* 12:293-307, 1927.
- Sokoloff, M. J., and Stewart, H. L.: Hyperplastic sclerosis of the pulmonary artery and arterioles: report of a case with discussion of pathogenesis. *Arch. Int. Med.* 51:403-412, 1933.
- Clark, E., and Graef, I.: Chronic pulmonary arteritis in schistosomiasis mansoni associated with right ventricular hypertrophy: report of case. *Am. J. Path.* 11:693-706, 1935.
- Shaw, A. F. B., and Ghareeb, A. A.: The pathogenesis of pulmonary schistosomiasis in Egypt with special reference to Ayerza's disease. *J. Path. & Bact.* 46:401-424, 1938.
- Rosenthal, S. R.: Sclerosis of pulmonary artery and arterioles clinical pathologic entity. *Arch. Path.* 10:717-739, 1930.
- Moller, P.: Studien über embolische und autochthone Thrombose in der Arteria pulmonalis. *Beitr. z. path. Anat. u. z. allg. Path.* 71:77, 1923.
- Apert, E., and Baillet, P. C.: Athérome généralisé de l'artère pulmonaire et de ses branches en coincidence avec une bécasse du trou de Botal chez une fille de treize ans. *Arch. de med. d. enf.* 35:141-152, 1932.
- Parker, F., Jr., and Weiss, S.: The nature and the significance of the structural changes in the lungs in mitral stenosis. *Am. J. Path.* 12:573-598, 1936.
- Goedel, A.: Zur Kenntnis der Veränderungen der rechten Herzens und schwerer Kreislaufstörung. *Virchows Arch.* 1930.
- Krutzsch, G.: Ueber rechtsseitige Herzhypertrophie durch Einengung des Gesamtquerschnittes der kleineren und kleinsten Lungenarterien. *Frankfurt Ztschr. f. Path.* 23:247-271, 1920.
- Schmidt, M. B.: cited by Krutzsch.²⁸
- Frothingham, C.: A case of extensive bilateral progressive thrombosis of the smaller branches of the pulmonary arteries. *Am. J. Path.* 5:11-22, 1929.
- Case records of the Massachusetts General Hospital: Case 23511. *New Eng. J. Med.* 217:1045-1049, 1937.

REPORT ON MEDICAL PROGRESS

THE TREATMENT OF JUVENILE DIABETES MELLITUS

ALLAN M. BUTLER, M.D.*

BOSTON

THE recent advances in the knowledge of the abnormal physiology of experimental diabetes mellitus, which have been reviewed in earlier progress reports,¹ have altered profoundly concepts of the disease,¹⁻¹² but as yet have not added to the therapeutic armamentarium that was available to the clinician four years ago. Present therapy is based almost entirely on the concepts of fifteen to twenty years ago concerning the derangement of carbohydrate,¹³ salt and water metabolism,¹⁴⁻¹⁷ and on the insulin provided by Banting and Best in 1922 and the protamine zinc insulin that followed Hagedorn's introduction of protamine insulin in 1935.¹⁸

The progress of the conflict between the proponents of low-carbohydrate and high-carbohydrate diets has remained veiled in the misty arguments of the past two decades and has only occasionally been visualized in the light of modern physiology and therapy. The clear-cut experiments of Conn and Newburgh¹⁹ on the effect of iso-glucogenic quantities of protein and carbohydrate on the blood

sugar have seemingly attracted little notice from either camp. The contributions of Lawrence and Archer²⁰ and Campbell and his co-workers²¹ on the relation between diet and the action of protamine zinc insulin have provided impressive evidence of

TABLE 1. *The Relation between the Carbohydrate in the Diet and the Effectiveness of Protamine Zinc Insulin.*

TEST PERIOD	DAILY CARBOHYDRATE CONTENT	DAILY CALORIC CONTENT	DAILY DOSAGE OF INSULIN*	RANGE OF BLOOD SUGAR	RANGE OF GLUCOSE IN 24 Hrs URINE
days	gm.	cal.	units	mg./100 cc.	gm.
10	160	±1800	10R-16P	70-180	3-14
12	100	±1750	0R-14P	70-180	<1-3
8	125	±1800	0R-16P	125-210	7-39
10	125	±1800	4R-20P	90-190	2-19
5	190	±1900	10R-20P	80-230	12-27

*Given before breakfast. R=plain insulin; P=protamine zinc insulin.

the effectiveness of this type of insulin in conjunction with low-carbohydrate intake but have not disturbed the clinician's allegiance to the cause of high-carbohydrate regimes.

A pertinent example is provided from the diabetic clinic of the Infants' and Children's Hos-

*Assistant professor of pediatrics, Harvard Medical School; assistant visiting physician, Infants' and Children's Hospitals.

pitals, Boston. The data in the accompanying table illustrate the increased effectiveness of protamine zinc insulin with a low-carbohydrate intake and the excellent control attainable on a low-carbohydrate, protamine insulin regime. Yet in spite of such evidence, I have continued for the simple, and perhaps invalid, reason of practical expediency to remain among the ranks of the many who prescribe diets that contain, according to the age of the patient, from 125 to 200 gm. of carbohydrate. Such diets are probably the most commonly used today. They require for adequate diabetic management of most juvenile* patients the use of both protamine zinc and plain insulin.^{†1, 11, 21, 23-27} Even then, considerable glycosuria occurs after at least one meal each day, unless the insulin is given more than once daily. The fact that most authorities do not commonly employ another dose of plain insulin before the particular meal‡ that is followed by this glycosuria indicates that transient glycosuria and the daily urinary loss of between 5 and 15 gm. of glucose are in their opinion relatively harmless.^{1, 11, 18, 21, 23, 24, 28, 27, 29, 30}

For if this opinion were not held, patients should be on either a low-carbohydrate diet with protamine zinc insulin once a day, or a liberal-carbohydrate diet with protamine zinc insulin once and plain insulin twice daily.

Because almost perfect control in most cases may be provided by either of these procedures, there seems to be little reason for resorting to the elaborate and inconvenient regime involving multiple injections of plain insulin.³¹ Moreover, the desirability of providing some protamine zinc insulin in the daily therapy is evidenced by the fact that transient ketosis, hypercholesterolemia and enlargement of the liver from excessive storage of glycogen are not encountered in patients receiving some insulin in this form.^{26, 30, 32, 33} The early morning hyperglycemia that used to be so troublesome with plain insulin alone is easily controlled by the administration of a portion of the total insulin in the form of the protamine preparation.^{1, 11, 18, 21, 23-27, 30, 33}

The early unfavorable experiences with the use of protamine insulin are seldom encountered today.^{1, 11, 18, 21, 23-26, 29, 30, 33, 34} There is now a wider appreciation of the fact that Hagedorn¹⁸ introduced the use of protamine insulin in conjunction with diets relatively low in carbohydrate and that protamine zinc insulin is relatively ineffectual in

reducing the daytime glycosuria of patients on high-carbohydrate diets unless the protamine insulin is supplemented with adequate plain insulin. The realization that young children require a higher ratio of plain insulin to protamine insulin than do older patients has increased the effectiveness of combined therapy in the younger group. Consequently the administration of excessive doses of protamine insulin with continued glycosuria during the day and the occurrence of annoying headaches or of severe insulin reactions between 2 a.m. and breakfast has disappeared from current practice.

Thus, in this four-year interim, when the advances in scientific knowledge have not been applicable to the clinical treatment of diabetes, the clinician has learned much about the art of applying available knowledge. Knowing that all diabetic infants and children require insulin, he no longer attempts to determine "carbohydrate tolerance" by graded diets, but places the patient, as soon as possible, on a routine diet and then administers the amount of insulin required for adequate control. Whether the carbohydrate content of the diet is low or high, experience has shown the advantage of immediately prescribing a dose of plain insulin and one of protamine zinc insulin that is lower than that which would result in hypoglycemia during the next twenty-four hours, and of supplementing this with doses of plain insulin, as indicated by the urine-sugar, or if necessary, by the blood-sugar concentrations. Using the general principle that the protamine insulin should be used to control the early morning blood sugar and the plain insulin to control the blood sugar during the day, the clinician can determine, in the course of five or six days, the before-breakfast dose of each type of insulin required for the control of each patient. He is further guided by the knowledge that a low-carbohydrate diet requires little and possibly no plain insulin, whereas for a young child a liberal-carbohydrate diet usually necessitates approximately equal amounts of each kind of insulin. When using a regime of the latter type, he knows that 15 to 20 gm. of carbohydrate should be taken in the midmorning to prevent hypoglycemia before the midday meal. Once the patient is adjusted to the routine diet and the daily before-breakfast insulin therapy, the physician controls the minor fluctuations in sugar balance due to infection or to the emotional stresses and strains of everyday life by slightly increasing or decreasing the dosage of plain insulin. If, during a period of temporary imbalance, hyperglycemia persists for several days, so that urine specimens taken before supper show too much sugar, an in-

*The word juvenile is used not so much to designate the age group, as to indicate that this progress note is not concerned with the type of diabetes that in older people appears to result from a glycogenic dysfunction associated with adiposity.³²

†"Plain insulin" is used to designate both amorphous insulin and crystalline insulin, since there appears to be no difference of clinical importance in the action of these two preparations.³⁰

‡The evening meal, if the insulin is given before breakfast.

jection of from 4 to 8 units of plain insulin before the evening meal may be prescribed. Insulin so given is not only very effective in controlling temporary hyperglycemia, but also unlikely to cause serious hypoglycemia and the possible reactions, which accumulating evidence³⁵⁻³⁸ indicates should not be considered lightly.

From these general considerations, the physician, to facilitate the patient's independent control of his diabetes, on the usual regime of liberal diet and both types of insulin before breakfast, provides some such rules of thumb as the following:

Symptoms of an insulin reaction between 10:30 a.m. and dinner in the middle of the day are the result of too little midmorning food or too much plain insulin. If reactions occur at this time and sufficient midmorning food is being taken, the dose of plain insulin should be reduced by 2 to 4 units, depending on the number of units taken before breakfast.

Symptoms of an insulin reaction between 2 a.m. and breakfast are the result of too much protamine zinc insulin and make it necessary to reduce the dose of protamine zinc insulin by 2 to 4 units, depending on the number of units taken before breakfast.

Reactions occurring late in the afternoon are the result of the combined effect of the plain insulin and the protamine zinc insulin—usually accentuated by exercise. When the diabetes is otherwise well controlled, they are best treated by giving midafternoon food in the form of fruit, fruit juice or bread, the last being taken from the bread of supper.

The appearance of too much sugar in the urine voided before the midday meal suggests the need of more plain insulin. However, before the dosage of insulin is increased, it is important to be certain that the sugar found in the specimen voided before the noon meal has not come into the bladder following breakfast. To make sure of this, it is necessary that the bladder be emptied some time between 10 and 11 a.m. If such a voiding has occurred, the sugar that appears in the urine before the noon meal is a fair index of the inadequacy of the dosage of plain insulin, which should then be increased by no more than 2 to 4 units at a time.

Too much sugar in the urine before breakfast suggests the need of more protamine zinc insulin. However, before sugar in the urine at this voiding is considered as an indication for increasing the dose of protamine zinc insulin, the possibility that this sugar might have come into the bladder the preceding evening should be checked. If there has been a voiding after 11 p.m., the repeated finding of sugar in the urine before breakfast is an indication for increasing the protamine zinc insulin. If there has been no voiding since earlier in the evening, judgment concerning the adequacy of the dose of protamine zinc insulin should await the analysis of a second voiding before breakfast. If the second specimen obtained—by having the patient drink one or two glassfuls of water—during the next three quarters of an hour contains sugar, the dose of protamine zinc insulin may be increased by 2 to 4 units.

The appearance of too much sugar in the urine due to an infection or to some other temporary disturbance is best controlled by a small amount of plain insulin before supper. An adequate supplementary dose of this type is 4 to 8 units, depending on the amount of the routine dose administered before breakfast.

In the treatment of coma, the clinician now utilizes the advantages incident to the immediate use of protamine zinc insulin and plain insulin, and of enough parenteral sodium lactate in the initial parenteral-fluid therapy to correct the hyperventilation, and so put the patient at rest in the first hour of therapy and pave the way to recovery within six to eight hours. The appropriate parenteral-fluid therapy can be estimated by the clinical appraisal of the degree of dehydration and acidosis, and can be administered without elaborate physiological calculations or chemical analysis.³⁹

Thus has the physician advanced the art of effective and economical medical care with the tools that have been made available. He need not be ashamed of his accomplishment, but he cannot be satisfied with it. He still ponders the old question: Should it be a high-carbohydrate or a low-carbohydrate diet? Eagerly, he awaits the answer from such work as that of Best and his co-workers,¹² which thus far not only casts doubt on the validity of the widely accepted but unproved theory that the high-carbohydrate regimes of today favor the insulinogenic capacity of the pancreas, but also suggests that the glycosuria and hyperglycemia of such regimes inhibit the recuperative power of the cells of the pancreatic islets. Often he worries: will our present degree of control of diabetic patients, which prevents transient ketosis, hypercholesterolemia, enlargement of the liver and appreciable glycosuria, prevent in the future such diabetic cardiovascular diseases as have occurred in the past? And while he wonders, he scans with hope the newer knowledge of the pituitary⁶ and adrenal⁹ hormones and of the cellular enzymes,⁷ for there new means of therapy may lie untouched.

REFERENCES

- 1 Joslin, E. P., Root, H. F., White, P., and Marble, A. Diabetes mellitus. *New Eng J Med* 221:173-178, 1939.
- 2 Joslin, E. P. Diabetes mellitus. *New Eng J Med* 223:21-27, 1940.
- 3 Houssay, B. A. Diabetes as a disturbance of endocrine regulation. *Am J Med Sc* 193:581-606, 1937.
- 4 Young, F. G. Permanent experimental diabetes produced by pituitary (anterior lobe) injections. *Lancet* 2:372-374, 1937. The diabetogenic action of crude anterior pituitary extracts. *Biochem J* 32:513-523, 1938.
- 5 Richardson, K. C., and Young, F. G. Histology of diabetes induced in dogs by injection of anterior pituitary extracts. *Lancet* 1:1098-1100, 1938.
- 6 Warren, S. *Pathology of Diabetes Mellitus*. Second edition. 246 pp. Philadelphia: Lea & Febiger, 1938.
- 7 Young, F. G. Anterior pituitary gland and diabetes mellitus. *New Eng J Med* 221:635-646, 1939.
- 8 Cori, C. F. Glycogen breakdown and synthesis in animal tissue. *Endocrinology* 26:285-296, 1940.
- 9 Soskin, S. The liver and carbohydrate metabolism. *Endocrinology* 26:297-308, 1940.
- 10 Long, C. N. H., Katzin, B., and Fry, E. G. The adrenal cortex and carbohydrate metabolism. *Endocrinology* 26:309-344, 1940.
- 11 White, P. Endocrine manifestations in juvenile diabetes. *Arch Int Med* 63:39-53, 1939.
- 12 Wilder, R. M., and Rutledge, D. I. Diseases of metabolism and nutrition. Review of certain recent contributions. I. Diseases of metabolism. *Arch Int Med* 63:356-385, 1939.
- 13 Haist, R. E., Campbell, J., and Best, C. H. The prevention of diabetes. *New Eng J Med* 223:607-615, 1940.
- 14 Macleod, J. J. R. *Carbohydrate Metabolism and Insulin*. 357 pp. London and New York: Longmans, Green and Co., 1926.

- 14 Archley D W, Loeb R T, Richards D W, Jr, Benedict E M, and Driscoll M E. On diabetic acidosis: a detailed study of electrolyte balances following the withdrawal and re-establishment of insulin therapy. *J Clin Investigation* 12:297-326 1933
- 15 Hartmann A F and Darrow D C. Chemical changes occurring in the body as the result of certain diseases. III. Composition of the plasma in severe diabetic acidosis and the changes taking place during recovery. *J Clin Investigation* 6:257-276 1928
- 16 Peters J P, Kydd D M, Eisenman A J, and Hild P M. The nature of diabetic acidosis. *J Clin Investigation* 12:377-391 1933
- 17 Dill D B, Bock A V, Lawrence J S, Talbot J H, and Henderson L J. Blood as a physicochemical system. VIII. Diabetic coma. *J Biol Chem* 81:551-574 1929
- 18 Hagedorn H C, Jensen B N, Kjarup N B, and Wodstrup J. Protamine insulinate. *J A M A* 106:177-180 1936
- 19 Conn J W, and Newburgh L H. The glycemic response to isoglycogenic quantities of protein and carbohydrate. *J Clin Investigation* 15:665-671 1936
- 20 Lawrence R D, and Archer, N. Some experiments with protamine insulinate. *Brit M J* 1:747-749, 1936
- 21 Campbell W R, Fletcher A A, and Kerr R B. Protamine insulin in the treatment of diabetes mellitus. *Am J M Sc* 192:589-600 1936
- 22 Newburgh L H, and Conn J W. A new interpretation of hyperglycemia in obese middle aged persons. *J A M A* 112:7-11 1939
- 23 Mosenthal, H O, and Mark M F. The prolonged use of protamine zinc insulin. *J A M A* 113:17-22 1939
- 24 Walker P, and Butler A M. Successful use of protamine zinc insulin in the treatment of diabetic girls. *J A M A* 112:1440 1939
- 25 Boyd G. Treatment of diabetes in children. *Canad M A J* 42:438-442 1940
- 26 Ricketts H T, and Wilder R M. Solutions of amorphous insulin and solutions of zinc insulin crystals: clinical studies on the comparative speed and duration of action. *J A M A* 113:1310-1312, 1939
- 27 Tolstoi E, and Weber F C, Jr. Protamine zinc insulin: a metabolic study. *Arch Int Med* 64:91-104 1939
- 28 Rahnowitch I M, Foster J S, Fowler A F, and Corcoran A C. Clinical experiences with protamine zinc insulin and other mixtures of zinc and insulin in diabetes mellitus. *Canad M A J* 35:239-252 1936
- 29 Jackson R L, Boyd J D, and Smith T E. Stabilization of diabetic child. *Am J Dis Child* 59:332-341 1940
- 30 Hansen P. Enlargement of the liver in diabetes mellitus. *J A M A* 106:914-916 1936
- 31 White P. Protamine insulin in the treatment of juvenile diabetes. *South M J* 31:15-21 1938
- 32 Wilder R, Jr. Why diabetics discontinue protamine insulins. *Am J M Sc* 197:557-559 1939
- 33 Soskin S. Physiologic action of insulin in shock therapy. *Arch Neurol & Psychiat* 42:563 1939
- 34 Wortis J, and Lambert R H. Irreversible or hyperglycemic insulin coma: its cause and its response to blood transfusion. *Am J Psychiat* 96:335-345 1939
- 35 Saks A L, and Alexander L. Fatal hypoglycemia: clinicopathologic study. *Arch Neurol & Psychiat* 47:286-297 1939
- 36 Baker A B. Cerebral lesions in hypoglycemia: experimental investigations. *Arch Path* 28:298-305 1939
- 37 Butler A M. Electrolyte and water balance. *New Eng J Med* 220:827-834 1939 P 831

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 26481

PRESENTATION OF CASE

A seventy-year-old housewife entered the hospital complaining of pain in the legs and back.

Eighteen months before admission, after a day of strenuous housecleaning, the patient developed a moderately sharp pain in the left hip that radiated down the posterior aspect of the leg to the heel. This pain remained constant for the next few days, and although troublesome, it did not interfere with work or sleep. Then it became intermittent, recurring every week for the next seven months and finally disappearing within a few weeks thereafter. She remained symptom free until six months before admission, when the pain reappeared in a less severe form; it was aggravated by activity but completely relieved by rest, and was accompanied by a dull ache in the lower back. Two weeks later the patient noticed a similar, radiating pain in the right hip that was constant and alternately dull and sharp. During the next few months the pain increased, but she continued to work. One night, five weeks before admission, while getting into bed she heard a "click" in the lower spine, followed by a painful, involuntary muscle spasm involving first the right then both legs, with the result that they were flexed on the abdomen. The spasm relented and recurred many times during the night, and she suffered from pain in the hips, groin, buttocks and legs. The attacks of muscle spasm decreased in number, and within a few days she was able to get about the house, and, indeed, preferred to sit upright, for lying flat caused unbearable paroxysms of pain. During this time the legs felt "numb and prickly." Two weeks before admission, when the patient entered another hospital, muscle spasm still occurred several times a day, lasted a few minutes and was followed by soreness of the leg muscles and lower abdomen. The attacks were precipitated by turning in bed, and the patient consequently remained on her back, with the result that a sacral bed sore developed. There were no accompanying constitutional symptoms, but she had lost 15 pounds in the few months prior to entry.

The patient had suffered from scarlatina at nine

years of age and had had frequent sore throats in her youth and intermittent psoriasis since childhood. At twenty-one she spent three months in bed because of "bronchitis" characterized by a low fever, cough and blood-streaked sputum. Her physician said she had "a spot on her left lung." There had been no recurrence of this illness.

Physical examination showed a well-developed and well-nourished woman in no acute distress. There was a psoriatic desquamation over the elbows and wrists. Each sclera showed an arcus senilis, and the fundi minimal arteriolar sclerosis. Examination of the heart and lungs was negative; the blood pressure was 160 systolic and 90 diastolic. Examination of the abdomen was negative, although one examiner believed that there was a vague nontender mass in the right upper quadrant. A 7-cm. ulcer with a gray, oozing base was present over the sacrum. Neurological examination was negative except that the left knee jerk was more active than the right. Rectal examination was negative; vaginal examination revealed a marital introitus and a smooth, soft, atrophic cervix. The fundus could not be felt, and the vaginal vaults were clear.

The temperature was 99°F., the pulse 103, and the respirations 20.

Examination of the urine showed a + test for albumin, and a negative test for Bence-Jones protein on five occasions. Examination of the blood showed a red-cell count of 5,280,000 with a hemoglobin of 14.1 gm. (photoelectric-cell technic), and a white-cell count of 9900 with 72 per cent polymorphonuclears. No plasma cells were seen. The sedimentation rate was 39 mm. in one hour. The nonprotein nitrogen of the blood was 23 mg. per 100 cc., and the serum protein 7.4 gm. The serum calcium was 10.9 mg. per 100 cc., the phosphorus 4.3 mg., and the phosphatase 6.8 units. A blood Hinton test was negative. A tuberculin test was negative in a dilution of 1:10,000, but positive in 1:1000, the area of induration and erythema measuring 1.5 cm. in diameter. Agglutination tests were negative for *Eberthella typhi*, *Salmonella paratyphi*, *S. schottmüller* and *Brucella abortus*. Examination of the stools was negative.

X-ray examination of the spine showed obliteration of the joint between the twelfth dorsal and first lumbar vertebrae, and extensive destruction of the inferior margin of the body of the twelfth dorsal and of the superior portion of the body of the first lumbar vertebra. The bones of the vertebrae were unusually dense, but there was very little new-bone formation about their margins. There was a paravertebral mass on the left side, extending from the level of the ninth

dorsal to that of the second lumbar vertebra, and a similar slightly lower mass on the right. Roentgenograms of the other vertebrae, the skull and chest were negative. A comparison of these films with those taken elsewhere showed no appreciable advance in the destructive process.

An intravenous pyelogram taken with a portable machine showed prompt excretion of the dye on both sides. Both renal pelves and calyces were moderately dilated, and there was a pressure defect in the pelvis and lower calyces on the left, produced by the paravertebral mass. In films taken approximately two months later, the medial portion of both kidney pelves showed a pressure defect. In some of the films there was also a suggestion of mass in the midpelvis.

The patient was placed in a Bradford frame, but continued to have attacks of muscle spasm and pain in the legs. The sacral ulcer gradually increased in size. Three weeks after admission she had an attack of nausea, vomiting and diarrhea that subsided within three days. At that time the knee and ankle jerks were equal, but hyperactive; the plantar reflexes were normal. A sternal puncture two months after admission showed a normal bone marrow. Nine weeks after admission, an aspiration and punch biopsy of the body of the twelfth dorsal vertebra was performed.

DIFFERENTIAL DIAGNOSIS

DR JAMES R. LINGLEY: The x ray films reveal a very definite process involving the twelfth dorsal and first lumbar vertebrae, with extensive bone destruction about the margins of the adjacent vertebral bodies, complete destruction of the intervertebral disk and marked increase in the density of both vertebral bodies. Some of the films show a suggestion of a soft tissue mass above the margins of the vertebrae, and possibly a little calcification in the mass. The other bones appear normal except for some decalcification.

DR CHARLES L. SHORT: The abstract says that there were two paravertebral masses. Are they quite definite?

DR LINGLEY: The one on the right is quite definite—the psoas muscle definitely bulges. I am not so sure about the one on the other side.

DR SHORT: Other films are said to show pressure defects, apparently from the paravertebral masses.

DR LINGLEY: There is a pressure defect in the left renal pelvis. That confirms the impression of a mass on the left. Although the pelvis is not well visualized, there seems to be a mass on the right. Hence, there are bilateral masses.

DR SHORT: The x ray findings will probably

give us the most valuable information for a diagnosis of this case. I should therefore like to summarize these findings, and Dr. Lingley will correct me if I am wrong. In the first place, there is a destructive spinal lesion that started, perhaps, in the intervertebral disk, but that may have started in one or the other of the two vertebrae. The paravertebral masses extend down, obstructing the kidney pelves. The other x ray films show no evidence of a primary lesion or of a primary infectious focus, and also no evidence of generalized bone disease. Apparently the only lesion was in the spine. I think the patient's history can also be explained on the basis of the x ray findings. There was pain in the legs from pressure on or irritation of the nerve trunks. The remission of four months in the course of the illness might have resulted from an inflammatory rather than a neoplastic lesion, although pressure effects from neoplasms may disappear temporarily. The flexion spasm of the legs can be explained by the involvement of the psoas muscles with the masses visible in the x ray films. One wonders on reading the history whether the patient was in danger of developing paraplegia, but examination in the hospital showed only suggestive evidence of pressure on the motor tracts—that is, the unequal knee jerks and, later, the increased knee jerks. A lumbar puncture was not made, probably wisely. There might have been danger of infection, because of the presence of the bed sore, or even of going through one of the paravertebral lesions. There is no mention of the examination of the spine in the physical examination. I suppose that it was not believed to be helpful, but we should like to know whether there were any local findings.

DR TRACY B. MALLORY: There is no note about the spine in the record of the physical examination, or even in the notes made after her transfer to the Orthopedic Service.

DR SHORT: I assume that there was some rigidity in the back and some tenderness. I do not believe that one can bring the psoriasis into the differential diagnosis. Certainly this is not rheumatoid arthritis. The bronchitis that the patient had fifty years ago is of some interest. This evidently was before the days of x-rays, and we do not know whether it was a tuberculous or a nontuberculous process in the chest.

The laboratory work is helpful largely in ruling out possibilities. Apparently the people taking care of this patient thought first of a neoplastic process, and it is evident that they considered multiple myeloma a leading possibility. There was no Bence-Jones protein in the urine.

The serum protein was high, but probably within normal limits. There were no plasma cells in the blood smears, and no evidence of multiple lesions in the other bones. Finally a biopsy of the sternum was done, with negative findings. These things do not rule out multiple myeloma, of course, but taken together they present very strong evidence against it. There was no evidence of a primary focus, if the lesion represented a metastatic process.

If we do call this a neoplasm, it is difficult to account for the two paravertebral masses. Of course a tumor could spread in this way, but the most likely form of neoplastic process in this case, if there is one, is lymphoma, which could give a lesion resembling this one. However, we have no positive evidence. There were no enlarged lymph nodes, the spleen was not palpable, and the patient had gone on eighteen months without any sign of lymphoma elsewhere in the body. This does not rule out the diagnosis, but makes it unlikely.

I favor an infection, rather than a neoplasm, as explaining this picture—that is, a primary infection starting in either the vertebrae or the intervertebral disk and spreading so as to cause irritation of the psoas muscles and some obstruction to the outflow of the kidneys.

Another possibility is a neoplasm with secondary infection. I do not see how we can decide that point. We can hardly say that this is an acute osteomyelitis, because constitutional symptoms and so forth are lacking. I do not believe that even a more chronic infection like undulant fever could cause this picture for so long a time without the patient's having had some evidence of a febrile reaction, although a spinal lesion of this sort with secondary abscess formation is not uncommon in undulant fever.

There are other, more chronic, types of infection such as syphilis, and we have no way of completely ruling them out. But we do have a negative history and a negative blood Hinton test, which are unusual for a syphilitic lesion. A chronic osteomyelitis of the spine might give a picture like this, but one would expect a constitutional reaction at one time or another.

You will probably see that I am leading up to a diagnosis of tuberculosis. The chronicity, the lack of constitutional reaction, the location of the process and the secondary abscess formation, if these are abscesses, would make a diagnosis of tuberculosis quite likely if this patient were a child. We should consider that first in diagnosis. I do not know why there was more bone reaction

than we usually see in tuberculosis. Is that correct?

DR. LINGLEY: There is more than you would expect, although there is usually some reaction.

DR. SHORT: There is no such bone production as one sees with a pyogenic process. It would be a help to bring in, as the primary infection, the illness that the patient had at twenty-one years of age; but we have no way of doing that. Tuberculosis does occur at this age, and may involve the spine, but of course it is quite rare, although childhood forms such as tuberculosis of the lymph nodes and tuberculous peritonitis occur in old people. That is the diagnosis that I finally arrived at, but I should agree with those who took care of the patient that a biopsy would be very essential to getting the final answer.

A PHYSICIAN: Was there a chest film?

DR. LINGLEY: Yes; it was negative.

DR. JOSEPH S. BARR: I agree that tuberculosis is the most likely diagnosis in this case. The x-ray films show such an extensive lesion that the patient must have had it for a considerable length of time. The adult intervertebral disk has no blood supply, and consequently there cannot be a blood-borne infection in the disk. So far as we know pathologically, these lesions begin very close to the disk and destroy it by direct extension, secondarily invading the vertebral bodies on either side.

DR. BERNARD M. JACOBSON: I saw this patient about a month and a half or two months after she came in, and my studies furnished fairly conclusive evidence against multiple myeloma. The Orthopedic Service thought that metastatic carcinoma was the best bet. She was an old lady who wanted very much to go home, and just as she was about to be discharged, the service, after a good deal of urging, decided to do a punch biopsy.

CLINICAL DIAGNOSIS

Metastatic carcinoma?

DR. SHORT'S DIAGNOSIS

Tuberculosis of spine.

ANATOMICAL DIAGNOSIS

Tuberculosis of spine.

PATHOLOGICAL DISCUSSION

DR. MALLORY: The punch biopsy was successful in this case. Several fragments were obtained that showed tubercles in various stages, thus substantiating Dr. Short's diagnosis.

CASE 26482

PRESENTATION OF CASE

A thirty-six-year-old Italian cook entered the hospital after vomiting large quantities of blood.

Two years before admission, the patient began to suffer from epigastric pain, coming on one hour after meals, relieved by food or soda and accompanied by belching and a feeling of fullness. His physician made a diagnosis of peptic ulcer and prescribed a dietary regime and alkalies. The patient improved under this treatment, and within three months the pain disappeared. Eight months before admission, the epigastric pain returned, and one month later he vomited "about two quarts" of bright-red blood, after which the stools were tarry for a week. A gastrointestinal examination at this time showed an ulcer half way down the lesser curvature of the stomach. The patient was again placed on an ulcer regime and was able to return to work in one month. However, he gradually abandoned the diet and started to smoke and drink a great deal, with the result that the pain returned three months before admission. He ignored the symptoms until one month before admission, when the stools became tarry for a week. The patient then returned to his physician; another gastrointestinal examination showed little change in the ulcer, which was described as having a 1.5-cm. base. Ten days before admission he vomited blood, felt weak and exhausted and remained in bed, but still did not follow the diet faithfully. On the morning of admission, he suddenly felt weak and nauseated, and shortly afterward had a large hematemeses. Two hours later he vomited bright-red blood three times within forty-five minutes.

The patient had had indolent leg ulcers for some years. The family history was irrelevant.

Physical examination showed the patient to be well-developed, but poorly nourished and extremely pale. The skin was dry and showed evidence of recent loss of weight; the extremities were cold and clammy. Examination of the lungs was negative. The heart was not enlarged or irregular, but the sounds were weak and rapid, with a tick-tack quality. The pulse was barely perceptible; the blood pressure was 56 systolic, 35 diastolic. The abdomen was soft and well relaxed, with some tenderness low in the epigastrium. The patient had received $\frac{1}{2}$ gr. of morphine immediately before entry. The legs showed varices, with eczema, pigmentation and ulceration. Examination of the nervous system was negative.

The temperature was 98°F., the pulse 105, and the respirations 25.

Examination of the urine was negative. The blood showed a red-cell count of 1,950,000 with a hemoglobin of 49 per cent, and a white-cell count of 12,350. The nonprotein nitrogen of the blood serum was 25 mg. per 100 cc., the prothrombin time 16 seconds, and the cell volume 22.9 per cent. Four stool examinations were guaiac positive.

The patient was placed on a Sippy regime and was given five 500-cc. transfusions within the next six days. He improved satisfactorily, and the red-cell count rose to 3,360,000, the hemoglobin to 60 per cent. On the seventh hospital day he vomited 500 cc. of bright-red blood, and two days later an equal quantity, with a consequent drop in the red-cell count to 1,330,000 with a hemoglobin of 25 per cent. Once again the patient was guided up the Sippy ladder, and was given daily blood transfusions and intravenous fluid with added vitamins. On the eighteenth hospital day he had a transient but sudden acute attack of abdominal pain and passed a large quantity of gas by mouth and rectum. The following day three hematemeses occurred, with an approximate total loss of 800 cc. of blood. On the twentieth hospital day fluoroscopic examination showed a large crater on the lesser curvature of the stomach, approximately 4 cm. below the cardia, with marked surrounding induration. The stomach was filled with material consistent with blood, milk or tumor. On the same day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. EDWARD HAMLIN, JR.: This appears to be a definite case of gastric ulcer with recurring massive hemorrhages. Presumably when the patient entered the hospital he was placed on the Medical Service and was given a transfusion; when it was found that despite excellent medical care he continued to have hemorrhages, a surgical consultant was called, who agreed that the patient's best chance lay in surgery. The fluoroscopic examination was undertaken the day of operation to determine the exact site of the lesion and to exclude esophageal varices.

DR. AUBREY O. HAMPTON: This patient was not examined in the upright position because of his condition. These films were taken as he lay on the table. There is the crater of the ulcer—an apparently huge lesion on the lesser curvature. It is magnified because of the position in which it was taken and is probably only about 2.5 cm. in diameter. The mucosal folds 1 cm. away are normal; those next to it are invisible, due to edema

and swelling. The conclusion of the X-ray Department was that the lesion was benign but unusually large.

DR. HAMLIN: The only other diagnosis that we need consider carefully is carcinoma. There are other possibilities, but it would be an unjustifiable waste of time to discuss them. From a statistical point of view everything seems to be in favor of benign ulcer. The patient is in the proper age group for an ulcer. Carcinoma of the stomach in that position is said to occur in only 25 per cent of the cases, and massive hemorrhages, such as this patient had, are considered somewhat unusual. The early history of periodic pain relieved by food and soda and the long remission following dietary treatment are quite typical of ulcer. But during the last few months, even after entry to the hospital and thoroughly controlled medical care, the patient did not cease to bleed and the ulcer crater appears to have increased in size. Finally the x-ray report notes an area of induration about the crater.

The surgeon's real responsibility in such a case is not so much to make an accurate preoperative diagnosis as to consider the possibility of carcinoma so that he will be able to deal with it if he finds the slightest confirmatory evidence on exploration. With the increasing size of the lesion and the surrounding area of induration, I should say that the surgeon made a preoperative diagnosis of carcinoma of the stomach and that was what he found.

DR. TRACY B. MALLORY: Are there any other suggestions?

DR. RICHARD H. SWEET: Would you consider lymphoma? I am not proposing that as a diagnosis, but I have the impression that ulcerative lymphomatous tumors are apt to produce massive hemorrhage in the gastrointestinal tract.

DR. HAMLIN: Lymphomas and sarcomas both are supposed to.

DR. F. DENNETTE ADAMS: Does not the fact that he not only failed to improve but grew worse under presumably excellent medical treatment seem very good evidence that there was more than ulcer?

DR. HAMPTON: I should like to add that the X-ray Department cannot be expected to make the differential diagnosis in such a lesion.

DR. WILLIAM B. BREED: Of course if you make a diagnosis of cancer you are going against the figures a good deal. This is a fairly straightforward case, and I do not believe there is enough evidence to make one put cancer first.

DR. HAMLIN: My argument was based on the fact that with a definite diagnosis of ulcer one would do a somewhat different operation than if one believed there was a possibility of cancer, and in this particular case the latter is so prominent that, at the first corroborative sign, a radical resection of the omentum should be done.

DR. BREED: It is often difficult for the surgeon to make a diagnosis of cancer even on inspection and palpation.

DR. REGINALD H. SMITHWICK: This was an unusual and interesting case. Those of us who saw the patient thought that he probably had a benign ulcer, but we realized, of course, that it was unusual for a man of thirty-six years of age to bleed as excessively as he did after three weeks of medical treatment in the hospital. Of course his general condition was desperate before operation, and our chief concern was to decide what was the best procedure, rather than to speculate as to the true nature of the lesion. Certainly, from the medical course of the last three weeks, there seemed to be little possibility that the patient would survive on a continued Sippy regime. For that reason, we operated, realizing that his chances of surviving operation were also very slim. We thought that perhaps a reasonable explanation for the bleeding was the location of the ulcer, which was comparable with that of the persistent bleeding ulcers that one sees in the duodenum. In this case it was located exactly where the left gastric artery goes into the stomach, and it seemed possible that a large branch of the artery was in the base of the ulcer. One would therefore not have to assume cancer to explain the bleeding. When we operated, it was very obvious on exploration and palpation of this lesion that it was carcinoma. There were some large nodes that ran up along the left gastric vessels, and the ulcer did involve branches of the left gastric artery; furthermore, when we had freed up the stomach and omentum, we could palpate a small subserous nodule in the wall of the stomach about a centimeter or two above the upper border of the ulcer, which was further evidence that the lesion was malignant. The later finding necessitated taking out practically the whole stomach; this was a little more than we wished to do in a patient in this condition, but we could handle the situation in no other way.

CLINICAL DIAGNOSIS

Bleeding peptic ulcer.

DR. HAMLIN'S DIAGNOSIS

Carcinoma of stomach.

ANATOMICAL DIAGNOSIS

Carcinoma of stomach

PATHOLOGICAL DISCUSSION

DR MALLORY: The specimen that was received

in the laboratory showed a large area of ulceration, in the base of which several small eroded arteries were evident. The borders were hard and cartilaginous in consistence, and it was quite obvious that the ulcer was malignant. Microscopic examination showed a fairly well differentiated adenocarcinoma. The patient survived resection, and was sent home in fair condition

The New England Journal of Medicine

Formerly the
Boston Medical and Surgical Journal
Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE
ON PUBLICATIONS

Official Organ of
THE MASSACHUSETTS MEDICAL SOCIETY
THE NEW HAMPSHIRE MEDICAL SOCIETY
THE VERMONT STATE MEDICAL SOCIETY

EDITORIAL BOARD

Joseph Garland, M.D.	John P. Sutherland, M.D.
William B. Breed, M.D.	Stephen Rushmore, M.D.
George R. Minot, M.D.	Henry R. Viets, M.D.
Frank H. Lahey, M.D.	Robert M. Green, M.D.
Shields Warren, M.D.	Charles C. Lund, M.D.
George L. Tobey, Jr., M.D.	John F. Fulton, M.D.
C. Guy Lane, M.D.	A. Warren Stearns, M.D.
William A. Rogers, M.D.	Dwight O'Hara, M.D.

ASSOCIATE EDITORS

Thomas H. Lanman, M.D.	Donald Munro, M.D.
Henry Jackson, Jr., M.D.	

Walter P. Bowers, M.D., EDITOR EMERITUS
Robert N. Nye, M.D., MANAGING EDITOR
Clara D. Davies, ASSISTANT EDITOR

SUBSCRIPTION TERMS: \$6.00 per year in advance, postage paid, for the United States; Canada, \$7.04 per year; \$8.52 per year for all foreign countries belonging to the Postal Union.

MATERIAL for early publication should be received not later than noon on Saturday.

THE JOURNAL does not hold itself responsible for statements made by any contributor.

COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston, Massachusetts.

CHRISTMAS SEAL CAMPAIGN

THE National Tuberculosis Association and its numerous affiliated associations throughout the country have no support but the contributions that once a year are given—dollar by dollar, two by two, five by five—to enable this vast organization to continue its campaign for the protection of health, happiness and life.

The money contributed has helped the organized attack that has cut the death rate of tuberculosis to one quarter of what it was in 1907, when the Seals were first sold; it has financed one of the greatest health-education programs ever carried on in this country. Tuberculosis must be defeated by educating the people, because science has as

yet found no vaccine to prevent the disease, no drug for its cure.

Education, paid for by the Christmas Seal dollars, is the most effective vaccine. The money has also played a part in establishing clinics and in developing new methods of diagnosis; it has shown that early tuberculosis can be diagnosed, with the result that the hopelessness once associated with the disease has been largely dispelled.

In spite of these advances, however, the final victory is yet to be won. Tuberculosis is still the chief cause of mortality among people between fifteen and forty-five years of age. And it still kills one person every eight minutes.

The campaign must go on to ultimate success, which is possible within the next few decades. The advances already made in curing and controlling the disease emphasize the responsibility of the public for next year and the years to come.

Without financial support, the fight cannot continue. A few dollars a year at Christmas time are little enough to pay for the protection of the life and health of a nation.

GRENFELL'S MISSION

THE death of Sir Wilfred Thomason Grenfell brings attention to a dramatic achievement in the world of medicine. Those who have caught the spark of his enthusiasm and know his work intimately will carry on in confidence that only the first chapter is ended, and that what has been built will remain a permanent contribution to civilization in the North.

As a young physician, Grenfell saw the need of medical care for the scattered fishing population of the remote coasts of northern Newfoundland and Labrador. Convinced that his services would mean more to this pioneer fringe than to the dwellers in the city, where doctors are many, he went. And, in the people of the North, he saw self-reliance, simple and rugged virtues, generous hospitality and similar qualities rarely seen where life is easier. Others have practiced medicine in lonely places, but few have inspired such a host of

worshipping followers to build a great medical service.

Greenfell's personal qualities were extraordinary. The magnetism with which he drew young and old to his standard was almost without parallel. Many persons are kind-hearted, many are strenuous workers, many are abler executives and administrators than he; but it took something greater than any or all of these to make him what he was. A stalwart Briton, he had none of the stolid Anglo-Saxon in his make-up; his quick wit, his facile imagination, his keen vision—far more artistic than logical—all these marked him rather as Celtic in his traits. Combined in him were intensely warm humanity, the fire of enthusiasm and a spiritual philosophy of life, with a spark of true genius running through it all, which made him an altogether unique figure. He was deeply religious but without a trace of bigotry or cant, and the very practical character of religious devotion that he brought to bear on his medical work was the keynote of his life.

He told of finding a widow with starving children on the coast near where game abounded, and of giving her a shotgun and shells with which to provide meat for her family. "I thought that was the way to preach the Gospel to her," he said simply. He would give seed to those who would plant it and raise vegetables, and prizes for the best gardens. But he discouraged the giving of dole without responsibility, and compared this to food without vitamins, leading to paralysis.

If he was sometimes inconsistent and gave to the needy from his "discretionary fund," even to the point of pauperizing the recipients, it should be recalled that it is difficult for anyone to be "hard-boiled" and strictly businesslike when countering those in dire want, especially for one so brimming with kindness and compassion as he was. It is easy to forgive such a fault in one of his impulsive nature. But if the mission he created is to build a better civilization in the North, his wise doctrine of encouraging self-help and self-reliance must prevail.

OBITUARY

FRANCIS EDWARD PORTER

1844–1940

Dr. Francis Porter passed away on October 11, after a long debilitating illness. He was born in Scituate on August 28, 1844. His early education was received there, followed by four years at Wesleyan University, from which he graduated in 1869. He graduated from Harvard Medical School in 1872. The following year he interned at the Massachusetts General Hospital, and the next two years were devoted to postgraduate study at Vienna and other European medical centers. One of his most cherished recollections was his personal association with Lister in Edinburgh and with Pasteur in Paris. At this time these two scientists were just beginning their remarkable contributions to the scientific world.

In 1875 he opened an office for the practice of medicine in Auburndale, where he worked untiringly until 1920, when failing health and partial loss of sight necessitated discontinuance of professional activities.

Dr. Porter was a member of the original staff of the Newton Hospital, where he served as physician, later as surgeon, and from 1910 to 1920 as consulting surgeon. He was a trustee of the hospital from 1910 to 1920. In 1923 he was honored by having the addition to Dennison Ward named Porter Ward.

Dr. Porter gave gladly and freely of his time and strength for the care of the sick and afflicted. By example and advice he assisted many young men as they began the practice of medicine. His thorough training, academic and professional, supplemented by postgraduate study and coupled with years of experience, made him one of the outstanding members of the profession.

The medical profession of Newton mourns the passing of one of its most highly esteemed members, this grand old man of the "old school."

H. F. K.

L. H. J.

F. R. C.

MEDICAL EPONYM

FICK PRINCIPLE

Professor Adolf Fick (1829–1901), of Würzburg, discussed "Ueber die Messung des Blutquantums in den Herzventrikeln [The Measurement of the Amount of Blood in the Ventricles]" on July 9,

ates: (effective November 1, 1940) Gerald F. Houser, M.D. University of Toronto '28, instructor in preventive medicine; William H. Sweet, M.D., Harvard '36, assistant in neurosurgery; Everett I. Evans, M.D. '37, University of Chicago, research fellow in surgery; Ernest M. Morris, M.P.H. Harvard '38, instructor in public-health practice.

REPORT OF MEETING

NEW ENGLAND SOCIETY OF PSYCHIATRY

The regular fall meeting of the New England Society of Psychiatry was held at the Northampton State Hospital on Thursday, October 24. Approximately one hundred and fifty members attended.

The morning was given over to inspection of the hospital. Luncheon was served at 1 p.m. in the hospital cafeteria. Dr. Roy D. Halloran, Superintendent of the Metropolitan State Hospital, Waltham, Massachusetts, presided at the afternoon meeting, at which the following were elected to membership: Bessie F. Brown, Wrentham; Richard C. Cooke, Waltham; Emerick Friedman, Norwich, Connecticut; Patrick J. Meehan, Tewksbury; Margaret R. Simpson, Foxboro. Memorial resolutions were read regarding the deaths of the following: G. Alder Blumer, Providence, Rhode Island; Martin W. Peck, Boston; Mary Theresa Muldoon, Waverley.

Dr. D. Ewen Cameron, professor of neurology and psychiatry at Albany Medical School, Albany, New York, presented a very interesting paper entitled, "The Influence of the Times on the Teaching of Psychiatry." He emphasized the need for a reorientation of concepts made necessary by changing conditions of community life and by modern work on causative factors in abnormal mental states.

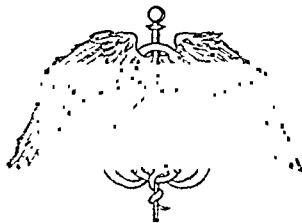
BARDWELL H. FLOWER, M.D., *Secretary.*

NOTICES

ANNOUNCEMENT

CHARLES A. ROBINSON, M.D., announces the removal of his office from 942 Broadway, South Boston, to 270 Commonwealth Avenue, Boston.

BOSTON DOCTORS' SYMPHONY ORCHESTRA



The Boston Doctors' Symphony Orchestra will rehearse under Alexander Thiede, formerly concertmaster of the Cleveland Symphony Orchestra, every Thursday at 8:30 p.m. Those interested in becoming members should communicate with Dr. Julius Loman, Pelham Hall Hotel, Brookline (BEA 2430).

HARVARD MEDICAL SOCIETY

The next meeting of the Harvard Medical Society will take place on Tuesday, December 10, in the amphitheater of the Peter Bent Brigham Hospital at 8:15 p.m.

PROGRAM

Presentation of cases.

The Relation of Forensic Medicine to Public Health. Dr. Thomas A. Gonzales, chief medical examiner, New York City.

JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston
Lecture Hall, 9-10 a.m.

MEDICAL CONFERENCE PROGRAM, DECEMBER-JANUARY

Tuesday, December 3—Case Study of Adrenal Deficiency in an Infant. Drs. F. C. McDonald and Nicholas Werthessen.

Wednesday, December 4—Hospital case presentation. Dr. S. J. Thannhauser.

Thursday, December 5—Vascular Disease as Seen in the Ocular Fundi. Dr. Benjamin Sachs.

Friday, December 6—Some Aspects of the Aging Heart. Dr. H. B. Sprague.

Saturday, December 7—Hospital case presentation. Dr. S. J. Thannhauser.

Tuesday, December 10—Some Geographical Differences in Surgical Diseases. Dr. Rudolf Nissen.

Wednesday, December 11—Hospital case presentation. Dr. S. J. Thannhauser.

Thursday, December 12—Pathogenesis of the So-Called "Metasyphilis" (General Paresis, Tabes). Dr. Alfred Hauptmann.

Friday, December 13—Clinicopathological conference. Dr. W. B. Castle.

Saturday, December 14—Hospital case presentation. Dr. S. J. Thannhauser.

Tuesday, December 17—The Clinical Significance of the Hypothalamus. Dr. Kurt Goldstein.

Wednesday, December 18—Hospital case presentation. Dr. S. J. Thannhauser.

Thursday, December 19—Title to be announced.

Friday, December 20—The Banti Syndrome. Dr. L. K. Diamond.

Saturday, December 21—Hospital case presentation. Dr. S. J. Thannhauser.

Medical conferences will be resumed Tuesday, January 7, 1941.

NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held on Thursday, December 5, at 7:15 p.m. in the classroom of the nurses' residence. There will be a moving-picture presentation of the clinical and biological evaluation of Gonadogen.

INTERNATIONAL COLLEGE OF SURGEONS

There will be a cancer clinic of the International College of Surgeons, New England Division, at the Westfield State Sanatorium, on Tuesday, December 10, at 2 p.m.

PROGRAM

Address of welcome. Dr. George S. Foster, of Manchester, New Hampshire.

Cancer of the Lip: Operative technic illustrated by slides. Dr. Ernest M. Daland, of Boston. Discussion by Dr. Stephen A. Cobb, of Sanford, Maine.

Diaphragmatic Complications Secondary to Tumors. Dr. John W. Turner, of Springfield. Discussion by Dr. Thomas F. Broderick, of Boston.

Embryonal Tumors of the Ovary. Dr. Alfred M. Glickman, of Springfield. Discussion by Dr. Edward S. Brackett, of Providence, Rhode Island.

The Detection of Bone Metastases by Means Other than X-ray. Dr. Robert Fienberg, of Westfield. Discussion by Dr. R. Nelson Hatt, of Springfield.

The Treatment of Rectal Malignancies with Demonstration of Cases. Dr. Frank H. Baehr, of Springfield. Discussion by Dr. James A. Gettings, of New Haven, Connecticut.

The Lynch Operation for Rectal Cancer (motion pictures). Dr. Jerome M. Lynch, of New York City. Discussion by Dr. Adam P. Leighton, of Portland, Maine.

Bladder Malignancies. Dr. James A. Seaman, of Springfield. Discussion by Dr. George P. Cheney, of New London, Connecticut.

The End Result of Surgery in Breast Cancer. Dr. William S. Bainbridge, of New York City.

Physicians are cordially invited to attend

CIETY MEETINGS AND CONFERENCES

LENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING
NDAY, DECEMBER 1

DAY, DECEMBER 2
12 15-1 15 p.m. Clinicopathological conference Peter Bent Brigham
Hospital amphitheater

DAY, DECEMBER 3
9-10 a.m. Case Study of Adrenal Deficiency in an Infant Drs F C
McDonald and Nicholas Wertheisen Joseph H Pratt Diagnostic
Hospital
12 15-1 15 p.m. Clinicorontogenological conference Peter Bent Brig
ham Hospital amphitheater

ONSDAY, DECEMBER 4
New England Obstetrical and Gynecological Society
9-10 a.m. Hospital case presentation Dr S J Thannhauser Joseph
H Pratt Diagnostic Hospital
12 m Clinicopathological conference Children's Hospital
2 p.m. New England Dermatological Society Boston City Hospital
2-4 p.m. Juvenile Drs Soma Weiss and E C Cutler Peter Bent
Brigham Hospital

THURSDAY, DECEMBER 5
8 30 a.m. Combined clinic of the medical surgical, orthopedic and
pediatric services of the Children's Hospital and the Peter Bent
Brigham Hospital, at the Peter Bent Brigham Hospital
9-10 a.m. Vascular Disease as Seen in the Ocular Fundi Dr Ben
jamin Sachs Joseph H Pratt Diagnostic Hospital
7 15 p.m. New England Hospital for Women and Children Monthly
clinical conference and meeting of the staff

FRIDAY, DECEMBER 6
9-10 a.m. Some Aspects of the Aging Heart Dr H B Sprague
Joseph H Pratt Diagnostic Hospital

TUESDAY DECEMBER 7
9-10 a.m. Hospital case presentation Dr S J Thannhauser Joseph
H Pratt Diagnostic Hospital

*Open to the medical profession

DECEMBER 3-21 — Joseph H Pratt Diagnostic Hospital Page 914
DECEMBER 4 — Wachusett Medical Society Page 876 issue of Novem
ber 21

DECEMBER 8-11 — American Academy of Dermatology and Syphilology
Page 831, issue of November 14

DECEMBER 10 — New England Society of Anesthesiology Page 743, issue
of October 31

DECEMBER 10 — Harvard Medical Society Page 914

DECEMBER 10 — International College of Surgeons Page 914

DECEMBER 12 — Pentucket Association of Physicians Page 263 issue of
August 15

DECEMBER 27-29 — National Convention of the Association of Medical
Industries Boston

JANUARY 4 1941 — American Board of Obstetrics and Gynecology Page
87, issue of November 7

MARCH 8 — American Board of Ophthalmology Page 201 issue of
August 1

APRIL 21-25 — American College of Physicians Page 10'5, issue of
June 20

MAY 21, 22 — Massachusetts Medical Society, Boston
JUNE 2-6 — American Medical Association Cleveland Ohio

DISTRICT MEDICAL SOCIETIES

ESSEX SOUTH

DECEMBER 4-MAY 14 — Page 831, issue of November 14

JANUARY 8 — Visceral Pain and Its Relief Dr James C. White Danvers
State Hospital, Hathorne

FEBRUARY 5 — Subject to be announced Lynn Hospital

MARCH 5 — X-ray in Heart Disease Dr Merrill C. Sisman Essex Sana
torium, Middleton

APRIL 2 — Pediatric Problems in General Practice Dr Joseph Garland
Addison Gilbert Hospital Gloucester

MAY 14 — Relation of the Doctor to the Law. Mr Leland Powers New
Ocean House, Swampscott

FRANKLIN

JANUARY 14

MARCH 11

MAY 13

Meetings will be held at 11 a.m. at the Franklin County Hospital,
Greenfield

NORFOLK

JANUARY 28 — Carney Hospital

FEBRUARY 25 — Medico Legal meeting 8 30 p.m. Hotel Puritan Boston.

MARCH 25 — To be announced

MAY 8 — Censors meeting Hotel Puritan

SUFFOLK

JANUARY 29 — Page 604 issue of October 10

APRIL 30 — Page 604, issue of October 10

WORCESTER

DECEMBER 11 — St Vincent Hospital, Worcester

JANUARY 8, 1941 — Worcester City Hospital Worcester

FEBRUARY 12 — Worcester State Hospital, Worcester

MARCH 12 — Memorial Hospital Worcester

APRIL 9 — Hahnemann Hospital, Worcester

Supper at 6 30 p.m. followed by a business meeting and scientific pro
gram.

BOOKS RECEIVED

The receipt of the following books is acknowl
edged, and this listing must be regarded as a suf
ficient return for the courtesy of the sender. Books
that appear to be of particular interest will be re
viewed as space permits. Additional information in
regard to all listed books will be gladly furnished
on request.

*A Pioneer Doctor in Old Japan: The story of John C.
Berry, M.D.* By Katherine Fiske Berry 8", cloth, 247 pp.,
with 20 illustrations. New York: Fleming H. Revell
Company, 1940 \$2.50

Laboratory Text in Pharmacology. By Robert P. Wal
ton, professor of pharmacology, University of Mississippi
School of Medicine 8", cloth, 85 pp. Philadelphia:
J. B. Lippincott Company, 1940 \$1.50.

The Diagnosis and Treatment of Cardiovascular Disease.
Volumes I and II. Edited by William D. Stroud, B.S.,
M.D., professor of cardiology, University of Pennsylvania
Graduate School of Medicine, and cardiologist to the Penn
sylvania, Graduate, Bryn Mawr, Abington Memorial,
St. Christopher's and Children's Heart hospitals. 4",
cloth, Volume I, 832 pp., with 163 illustrations, and Vol
ume II, 855 pp., with 153 illustrations Philadelphia: F. A.
Davis Company, 1940. \$18.00.

Obstetrics in General Practice. By J. P. Greenhill, B.S.,
M.D., professor of obstetrics and gynecology, Loyola Uni
versity School of Medicine, Chicago, professor of gynecol
ogy, Cook County Graduate School of Medicine, and
attending gynecologist, Cook County Hospital. 8", cloth,
448 pp., with 112 illustrations Chicago: Year Book Pub
lishers, Inc., 1940 \$3.50.

The Practice of Medicine. By Jonathan Campbell Meakins, M.D., LL.D., professor of medicine and director of the Department of Medicine, McGill University Faculty of Medicine, physician-in-chief, Royal Victoria Hospital, Montreal, formerly professor of therapeutics and clinical medicine, University of Edinburgh, fellow of the Royal Society of Edinburgh, fellow of the Royal Society of Canada, fellow of the Royal College of Physicians, London, fellow of the Royal College of Physicians, Edinburgh, honorary fellow of the Royal College of Surgeons, Edinburgh, and fellow of the Royal College of Physicians, Canada. Third edition. 4°, cloth, 1430 pp., with 562 illustrations, including 48 in color. St. Louis: C. V. Mosby Company, 1940. \$10.00.

Office Urology, with a Section on Cystoscopy. By P. S. Pelouze, M.D., assistant professor of urology, University of Pennsylvania School of Medicine, consulting urologist, Delaware County Hospital, special consultant to United States Public Health Service, and member of Board of Directors, American Social Hygiene Association and American Neisserian Medical Society. 4°, cloth, 766 pp., with 443 illustrations, 19 in color. Philadelphia: W. B. Saunders Company, 1940. \$10.00.

Advances in New York City's Health: Annual report of the Department of Health of the City of New York for 1939 with a review of developments from 1934-1939. John L. Rice, M.D., commissioner of health. New York: Department of Health, 1940. Complimentary.

Methods for Diagnostic Bacteriology: A complete guide for the isolation and identification of pathogenic bacteria for medical bacteriology laboratories. By Isabelle G. Schaub, A.B., assistant in bacteriology, Department of Pathology and Bacteriology, Johns Hopkins University School of Medicine, and M. Kathleen Foley, A.B., bacteriologist in charge of the Diagnostic Bacteriological Laboratory, Medical Clinic, Johns Hopkins Hospital, Baltimore. 8°, cloth, 313 pp. St. Louis: C. V. Mosby Company, 1940. \$3.00.

Borrowed Children: A popular account of some evacuation problems and their remedies. By Mrs. St. Loe Strachey. With a foreword by Amabel Williams-Ellis. 12°, cloth, 149 pp. New York: Commonwealth Fund, 1940. 75 cents.

The Rockefeller Foundation, International Health Division: Annual report, 1939. 8°, paper, 230 pp., with 15 illustrations. New York: The Rockefeller Foundation, 1940.

Dr. Colwell's Daily Log for Physicians: A brief, simple, accurate financial record for the physician's desk. 4°, cloth. Champaign, Illinois: Colwell Publishing Company, 1940. \$6.00.

BOOK REVIEWS

Frank Howard Lahey: Birthday volume, June 1, 1940. 8°, cloth, 466 pp., with 71 illustrations and 29 tables. Springfield, Illinois: Charles C Thomas, 1940.

To commemorate Dr. Frank H. Lahey's sixtieth birthday, his associates, friends and others have issued a volume of papers, largely surgical, covering a varied field. Since there is no index, the papers themselves will be of little value to the medical profession, and few librarians will find them of sufficient value or importance to catalogue the authors and titles separately. This is indeed unfortunate, for tucked away in volumes of this sort are rare gems, such, for example, as one by Ray Lyman Wilbur on "Mental Laundries," which is an essay on individual practice at its best.

In general, the work of the Lahey Clinic is reflected in the contributions to this volume. A large number deal with the surgery of the gastrointestinal tract. No paper describes the history of the clinic itself, except one about the neurosurgical service. One misses, too, any adequate report on Dr. Lahey and his important relations to the medical profession as a whole. The volume, therefore, in spite of being a splendid tribute, richly deserved, to one of the leaders of American medicine, is somewhat of a disappointment to the general reader.

The format is pleasing; a photograph of Dr. Lahey serves as a frontispiece, and there are numerous illustrations in association with the papers. References to the literature accompany most of the contributions.

Physiological Optics. By W. D. Zoethout, Ph.D. Third edition. 8°, cloth, 406 pp., with 214 illustrations. Chicago: Professional Press, 1939. \$5.00.

Of the several modern texts on physiologic optics, this book is probably the most appropriate for a cursory review of the subject. The third edition presents the orthodox material in an orthodox way. In avoiding controversy, it unfortunately gives the unwarranted impression of finality, but perhaps this is inevitable in view of the book's brevity. On the whole, it is a very readable introduction to the subject.

The Dream World: A survey of the history and mystery of dreams. R. L. Mégroz. 8°, cloth, 319 pp. New York: E. P. Dutton & Company, Inc., 1939. \$2.50.

This volume is an anthology of dreams and of dream literature, and at the same time, a summary of theories and historical material. It gives an account of the dreams and dream cults of savage and civilized people and of the popular literature on dreams from ancient to modern times. It demonstrates by quotation how this literature has often anticipated modern theories, and also how it emphasizes supernormal knowledge and telepathic communication.

It is well known, even outside the scientific literature of dreams, that the dream pursues the dreamer's waking interests. For instance, the Queen Mab speech in *Romeo and Juliet* or Petronius's statement that "each man makes dreams for himself" both show that dreams are wish-fulfillments. It is interesting, also, as the author points out, that Lincoln, who was liable to depressed moods and had frequent presentiments of a violent death, had a momentary anxiety-dream of his own assassination.

The author believes that the mystery of dreaming includes supernormal knowledge and extrasensory perception and emphasizes that dreams have become too much bound with psychotherapy and the analysis of unconscious motives. Freud's theory of dreams is referred to as "materialism in psychology," in spite of the fact that Freud reiterates that the dream is a subjective psychic production. In fact, the last chapter of Freud's *The Interpretation of Dreams* is entitled "The Psychology of Dream Activities." As for dreaming the future, careful analyses have shown that the dream originates from the past and touches on the future only by representing a wish as fulfilled; it is therefore in no sense "prophetic." There is no evidence, according to the scientific literature of dreams, that they bear any relation to telepathy.

As an anthology the volume is useful, but it does not attempt to solve any of the abstruse problems of dream psychology.

The New England Journal of Medicine

Copyright 1940 by the Massachusetts Medical Society

VOLUME 223

DECEMBER 5, 1940

NUMBER 23

CONGENITAL DIAPHRAGMATIC HERNIA*

WILLIAM E. LADD, MD AND ROBERT E. GROSS, MD†

BOSTON

THE problem of congenital diaphragmatic hernia in infancy is quite different from that of diaphragmatic hernia in later life. A review of the literature in 1931 by Hedblom¹ disclosed that 75 per cent of the patients with congenital diaphragmatic hernia died before the end of the first month of life. If this observation had excluded the cases of hernia through the esophageal opening, the mortality percentage would probably have been appreciably higher. In 1936, Orr and Neff in a very extensive review of the literature could find but 17 cases of congenital diaphragmatic hernia that had been operated on in the first year of life, in which only 9 of the patients survived. In the Children's Hospital there have been 25 of these cases, in 9 of the earlier ones the policy of delaying operative interference until the child grew older was adopted. Of these 9 patients, 5 are known to be dead, 3 cannot be traced, and only 1—who had a hernia through the esophageal opening—is known to be living. From these statements it must be apparent that there is little to recommend delayed or nonoperative treatment of diaphragmatic hernia in early life.

The situations in the diaphragm where congenital hernia occurs are the left and right sides posteriorly, where the defect is due to a persistent pleuroperitoneal canal (the foramen of Bochdalek), the esophageal opening, or the substernal opening commonly referred to as the foramen of Morgagni. Of these hernias, that occurring in a persistent pleuroperitoneal canal is by far the commonest. The fact that the hernia through the esophageal hiatus is commonest in adult life is due to the high mortality in infancy of patients with a hernia through the pleuroperitoneal canal.

The symptoms of diaphragmatic hernia may be respiratory, circulatory, digestive or a combination of all three, depending on the number of abdominal viscera in the thorax and on the size of the hernial ring. In a newborn infant showing cyanosis, dyspnea, or vomiting, diaphragmatic hernia is one of the conditions that should be considered. Cyanosis may be evident immediately after delivery. It may be transient and may appear only during nursing or crying, but in some cases it may be so severe that the constant use of an oxygen tent is necessary to sustain life. Vomiting may be only occasional or may follow most of the feedings. In patients surviving the neonatal period it is common to have poor weight gain or even weight loss.

Physical examination may show unduly rapid respiratory and pulse rates and a heart displaced away from the affected side. Percussion of the chest on the side of the hernia may be dull or tympanic according to whether there is fluid or air in the misplaced viscera. Auscultation may reveal absent or distant breath sounds and possibly intestinal gurgles that, if present, at once suggest the correct diagnosis. When the major portion of the alimentary tract is in the thorax, tympany is lacking on abdominal percussion, and the abdomen is scaphoid in appearance.

Roentgenological examination should always supplement the history and physical examination. A roentgenogram without the use of contrast media will usually give all the necessary information and is probably safer than giving barium to the baby. If, however, a barium meal is required, only a thin mixture should be used, because there is real danger of causing obstruction or aspiration by giving too thick a mixture to small infants.

The normal findings in the chest are greatly distorted by x-ray examination. The affected side contains viscera that are continuous with those in the abdomen. The mediastinal structures, including the heart, are pushed to the opposite side, and both lungs may be greatly compressed.

*Read in part before a combined meeting of the Philadelphia Academy of Surgery and the Boston Surgical Society, March 4, 1940.
†From the Department of Surgery, Children's Hospital, and the Department of Surgery, Harvard Medical School. This work was supported by a grant from the Coffrey M. Hyatt Trust.

Medical professor of surgery, Harvard Medical School; chief of the Surgical Service, Children's Hospital.

Associate in surgery, Harvard Medical School; associate visiting surgeon, Children's Hospital.

The Practice of Medicine. By Jonathan Campbell Meakins, M.D., LL.D., professor of medicine and director of the Department of Medicine, McGill University Faculty of Medicine, physician-in-chief, Royal Victoria Hospital, Montreal, formerly professor of therapeutics and clinical medicine, University of Edinburgh, fellow of the Royal Society of Edinburgh, fellow of the Royal Society of Canada, fellow of the Royal College of Physicians, London, fellow of the Royal College of Physicians, Edinburgh, honorary fellow of the Royal College of Surgeons, Edinburgh, and fellow of the Royal College of Physicians, Canada. Third edition. 4°, cloth, 1430 pp., with 562 illustrations, including 48 in color. St. Louis: C. V. Mosby Company, 1940. \$10.00.

Office Urology, with a Section on Cystoscopy. By P. S. Pelouze, M.D., assistant professor of urology, University of Pennsylvania School of Medicine, consulting urologist, Delaware County Hospital, special consultant to United States Public Health Service, and member of Board of Directors, American Social Hygiene Association and American Neisserian Medical Society. 4°, cloth, 766 pp., with 443 illustrations, 19 in color. Philadelphia: W. B. Saunders Company, 1940. \$10.00.

Advances in New York City's Health: Annual report of the Department of Health of the City of New York for 1939 with a review of developments from 1934-1939. John L. Rice, M.D., commissioner of health. New York: Department of Health, 1940. Complimentary.

Methods for Diagnostic Bacteriology: A complete guide for the isolation and identification of pathogenic bacteria for medical bacteriology laboratories. By Isabelle G. Schaub, A.B., assistant in bacteriology, Department of Pathology and Bacteriology, Johns Hopkins University School of Medicine, and M. Kathleen Foley, A.B., bacteriologist in charge of the Diagnostic Bacteriological Laboratory, Medical Clinic, Johns Hopkins Hospital, Baltimore. 8°, cloth, 313 pp. St. Louis: C. V. Mosby Company, 1940. \$3.00.

Borrowed Children: A popular account of some evacuation problems and their remedies. By Mrs. St. Loe Strachey. With a foreword by Amabel Williams-Ellis. 12°, cloth, 149 pp. New York: Commonwealth Fund, 1940. 75 cents.

The Rockefeller Foundation, International Health Division: Annual report, 1939. 8°, paper, 230 pp., with 15 illustrations. New York: The Rockefeller Foundation, 1940.

Dr. Colwell's Daily Log for Physicians: A brief, simple, accurate financial record for the physician's desk. 4°, cloth. Champaign, Illinois: Colwell Publishing Company, 1940. \$6.00.

BOOK REVIEWS

Frank Howard Lahey: Birthday volume, June 1, 1940. 8°, cloth, 466 pp., with 71 illustrations and 29 tables. Springfield, Illinois: Charles C Thomas, 1940.

To commemorate Dr. Frank H. Lahey's sixtieth birthday, his associates, friends and others have issued a volume of papers, largely surgical, covering a varied field. Since there is no index, the papers themselves will be of little value to the medical profession, and few librarians will find them of sufficient value or importance to catalogue the authors and titles separately. This is indeed unfortunate, for tucked away in volumes of this sort are rare gems, such, for example, as one by Ray Lyman Wilbur on "Mental Laundries," which is an essay on individual practice at its best.

In general, the work of the Lahey Clinic is reflected in the contributions to this volume. A large number deal with the surgery of the gastrointestinal tract. No paper describes the history of the clinic itself, except one about the neurosurgical service. One misses, too, any adequate report on Dr. Lahey and his important relations to the medical profession as a whole. The volume, therefore, in spite of being a splendid tribute, richly deserved, to one of the leaders of American medicine, is somewhat of a disappointment to the general reader.

The format is pleasing; a photograph of Dr. Lahey serves as a frontispiece, and there are numerous illustrations in association with the papers. References to the literature accompany most of the contributions.

Physiological Optics. By W. D. Zoethout, Ph.D. Third edition. 8°, cloth, 406 pp., with 214 illustrations. Chicago: Professional Press, 1939. \$5.00.

Of the several modern texts on physiologic optics, this book is probably the most appropriate for a cursory review of the subject. The third edition presents the orthodox material in an orthodox way. In avoiding controversy, it unfortunately gives the unwarranted impression of finality, but perhaps this is inevitable in view of the book's brevity. On the whole, it is a very readable introduction to the subject.

The Dream World: A survey of the history and mystery of dreams. R. L. Mégroz. 8°, cloth, 319 pp. New York: E. P. Dutton & Company, Inc., 1939. \$2.50.

This volume is an anthology of dreams and of dream literature, and at the same time, a summary of theories and historical material. It gives an account of the dreams and dream cults of savage and civilized people and of the popular literature on dreams from ancient to modern times. It demonstrates by quotation how this literature has often anticipated modern theories, and also how it emphasizes supernormal knowledge and telepathic communication.

It is well known, even outside the scientific literature of dreams, that the dream pursues the dreamer's waking interests. For instance, the Queen Mab speech in *Romeo and Juliet* or Petronius's statement that "each man makes dreams for himself" both show that dreams are wish-fulfillments. It is interesting, also, as the author points out, that Lincoln, who was liable to depressed moods and had frequent presentiments of a violent death, had a momentary anxiety-dream of his own assassination.

The author believes that the mystery of dreaming includes supernormal knowledge and extrasensory perception and emphasizes that dreams have become too much bound with psychotherapy and the analysis of unconscious motives. Freud's theory of dreams is referred to as "materialism in psychology," in spite of the fact that Freud reiterates that the dream is a subjective psychic production. In fact, the last chapter of Freud's *The Interpretation of Dreams* is entitled "The Psychology of Dream Activities." As for dreaming the future, careful analyses have shown that the dream originates from the past and touches on the future only by representing a wish as fulfilled; it is therefore in no sense "prophetic." There is no evidence, according to the scientific literature of dreams, that they bear any relation to telepathy.

As an anthology the volume is useful, but it does not attempt to solve any of the abstruse problems of dream psychology.

advantages that it possesses. Whatever anesthetic is employed, there must always be provision for giving positive pressure if the need should arise.

It is our practice to paralyze the phrenic nerve, through a small supraclavicular incision, on the affected side before attempting repair of the hernia. The purpose of this procedure is to facilitate the closure of the hernial opening and to prevent excessive strain on the suture line during healing of the diaphragmatic wound. Immediately after this one should proceed with the repair of the hernia. In one case we crushed the phrenic nerve; it once

sions, it is much easier to pull the abdominal contents out of the chest from below than to push them out from above. In fact, in 4 of our cases it would have been impossible to reduce the hernia through a thoracic approach, because the abdominal cavity was too small to receive all the viscera.

The abdominal incision may be vertical through the rectus muscle of the affected side, or subcostal; either type gives a satisfactory approach. In each of our cases a rectus incision afforded an excellent exposure of the diaphragm. The hernial ring should then be stretched so as to allow air to enter the thorax. If an attempt is made to draw the intestines out of the chest before doing this, they are usually sucked back again as fast as they are pulled out; however, after some air has been allowed to enter the thorax, they can be readily withdrawn from the thorax and placed outside the abdominal wall, where they are wrapped in warm, moist gauze. If the hernial ring is small, the viscera must be withdrawn in a particular sequence: on the right side the liver must be reduced last, and on the left side, the spleen.

The next step in the operation consists in denuding the edge of the hernial ring of its serous membrane. The exposed muscle edges are then approximated with one row of mattress sutures of silk, followed by a row of interrupted sutures of the same material, to approximate the peritoneal edges. A small urethral catheter is led through the diaphragmatic wound into the pleural cavity. Just before the final diaphragmatic sutures are tightened, gentle suction is applied to the catheter, which is then withdrawn. In this way the lung can be quickly expanded.

The abdominal viscera are next replaced in the peritoneal cavity, and the abdominal wound is closed in layers if there is not too much tension. It must be remembered that in many cases the abdominal cavity has not developed because it never contained all its viscera, and hence there is not sufficient room to accommodate them. This seems to be an insuperable difficulty, but it can be met first by undercutting the skin to allow it to slide, and next by cutting across the rectus muscle to allow the abdominal wall to stretch. One then closes only the subcutaneous fascia with a running suture of silk and the skin with interrupted silk mattress stitches. This of course leaves an incisional hernia, which can be repaired later when the abdominal wall has become sufficiently stretched. The optimum time for this is five or six days after the first operation. This two-stage plan has several advantages over making a prolonged effort at a one-stage closure of the abdominal wall in the usual layers, if the latter must be done under great tension; it is far less shocking; it avoids plac-

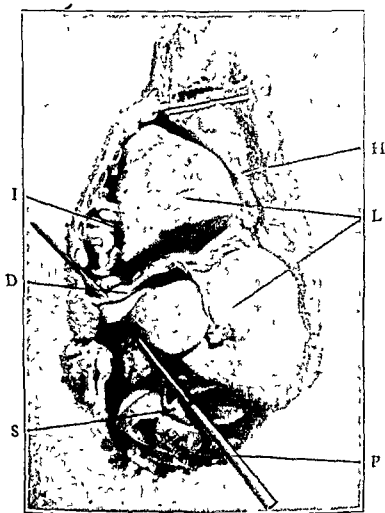


FIGURE 2.

Photograph of a post-mortem specimen showing a right-sided diaphragmatic hernia in a newborn child. The heart is displaced to the subject's left, and the left lung is greatly compressed. All the intestines are displaced up into the right pleural cavity. The liver has a deep fissure where it passes through the diaphragmatic opening. D = diaphragm; H = heart, I = intestine, L = liver; P = probe passing through the diaphragmatic opening; S = stomach.

operation, hoping to perform the hernial repair four or five days later, but the infant died before that time.

There seems to be a variance of opinion concerning the best surgical approach. We agree with Donovan³ that the abdominal approach has many advantages for the infant, whereas this may not be true for the adult. In infants, the occurrence of adhesions between the intestines and pleural structures is extremely rare. In the absence of adhe-

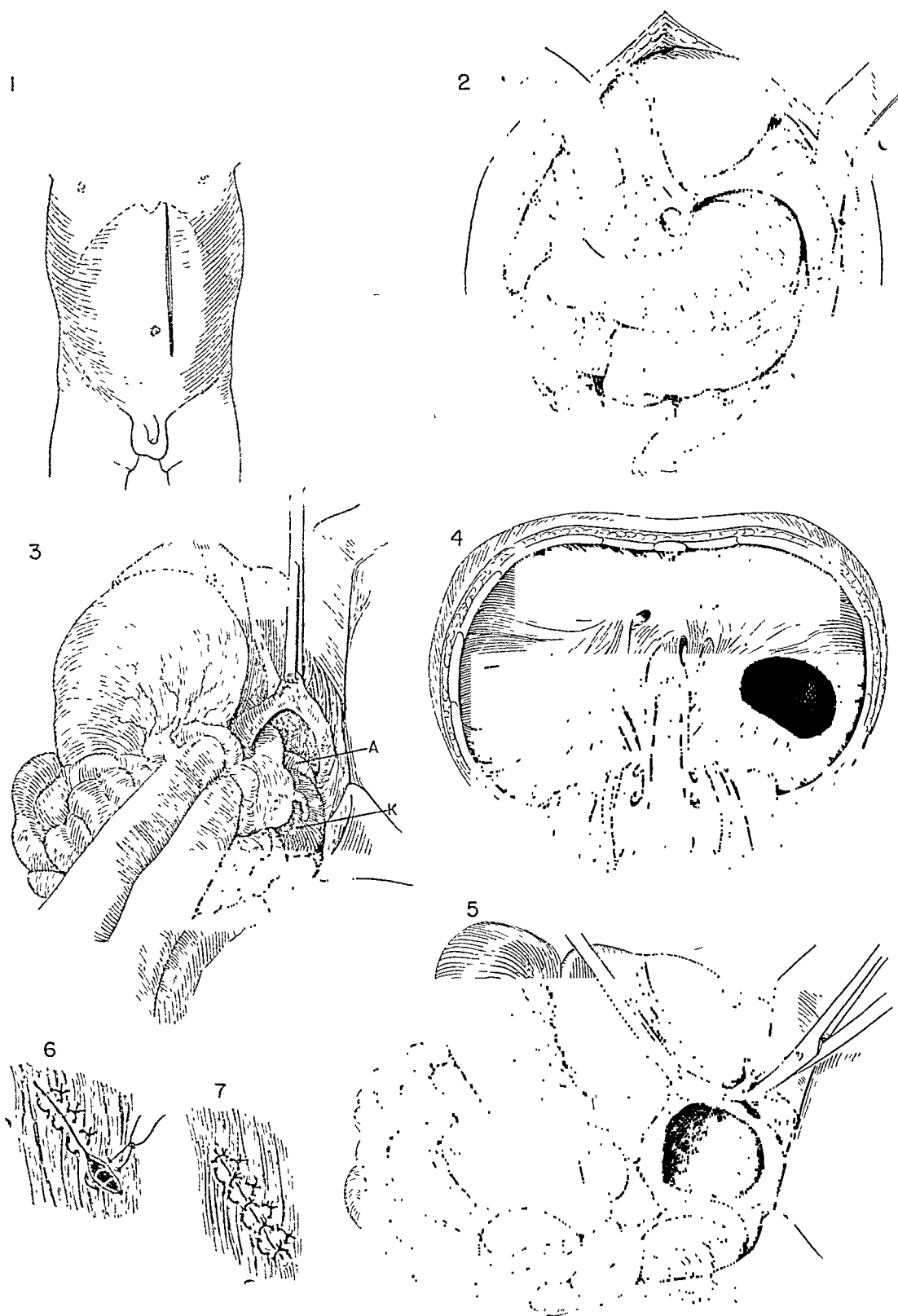


FIGURE 3.

Steps in the surgical repair of a left-sided diaphragmatic hernia of the type shown in Figure 1 and as exemplified in Cases 3, 5, 8 and 9. 1 = position of the abdominal incision; 2 = view obtained on opening the abdomen (the stomach and colon are seen projecting up through the diaphragmatic defect; all the intestines, except the duodenum, are in the thorax); 3 = withdrawal of abdominal opening in the left, posterolateral aspect of under surface of diaphragm to show position of the to make a raw edge; 6 = approximation of the diaphragmatic edges with interrupted mattress sutures of silk; 7 = reinforcement of peritoneal edges along the suture line with interrupted silk sutures; A = adrenal gland; K = kidney.

ing great strain on the suture line in the diaphragm; and it avoids embarrassment of the respiratory and circulatory systems.

Closing the abdominal wall is by far the most

anesthesia, the exposure of the diaphragmatic defect,—with an abdominal approach,—the reduction of the hernia, and the closure of the diaphragmatic openings have all been satisfactory, but the

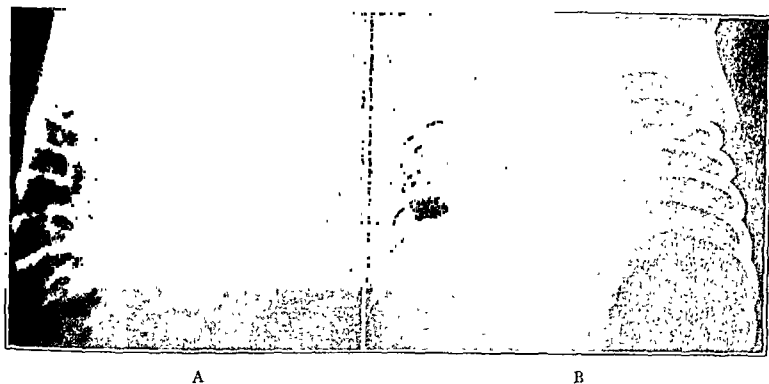


FIGURE 4. Case 6.

Roentgenograms of an eleven-day-old infant with right-sided hernia. A = preoperative film; B = film taken three weeks after operation.

difficult problem in the entire treatment of congenital diaphragmatic hernia. In our hands the

replacing and maintaining of viscera within the underdeveloped abdominal cavity still remained

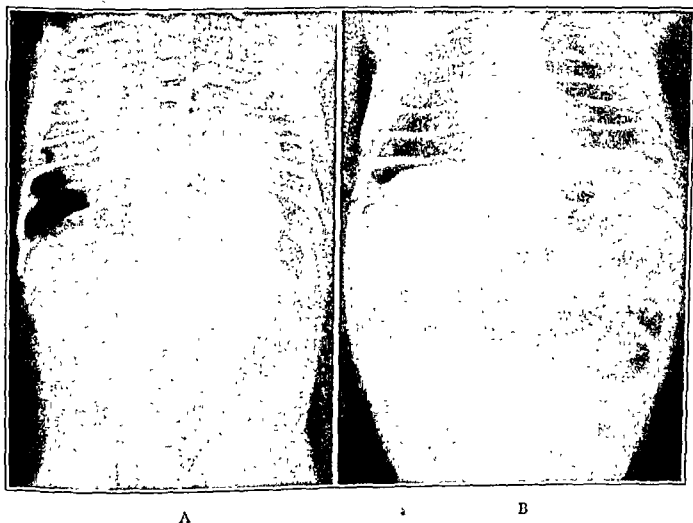


FIGURE 5. Case 8.

A = roentgenograms of a thirty-six-hour-old baby with left-sided hernia. The gas-filled intestines are in the thorax, with the heart displaced to the right and the right lung compressed; operation was performed at forty hours of age. B = film taken at one month of age, showing normal expansion of the lungs and return of the heart to normal position.

a problem until it was solved by the method of two-stage closure. In our early cases the abdominal wall was always completely closed in layers, in spite of the highly increased intraperitoneal pressure. This was probably one cause of the high mortality at that time.

The aftercare of these patients is important. They should be given a small blood transfusion at the end of the operation to replace any blood loss and to combat any hemorrhagic tendency of the newborn. The transfusion should be small enough to avoid any risk of embarrassing the right side of the heart, which in such cases is a very real danger. The infant is then placed in a tent with 90 to 95 per cent oxygen, for three reasons: first, to make breathing less labored; secondly, to keep the intestine deflated; and thirdly, to remove rapidly any room air which might have been trapped in the pleural cavity. Feeding is so regulated as to give an amount of fluid adequate to maintain water balance, but little attempt should be made to fulfill the caloric requirements for the first few days. If sufficient fluids cannot be given by mouth, they should be supplemented by parenteral fluids.

CASE REPORTS

The brief summaries of 4 cases are as follows:

CASE 2.* L. P., a girl, was born at full term and by a normal delivery. The birth weight was 7 pounds, 14 ounces. When feeding was attempted, the baby became cyanotic and choked. Vomiting often followed. This difficulty appeared to be more marked with breast than with artificial feeding. The patient was therefore removed from the breast and fed on a Lactogen formula. At that time a diaphragmatic hernia was suspected and confirmed by x-ray studies. For several weeks the baby continued to have cyanotic attacks when fed, and remained on the danger list at the maternity hospital. At the end of 3 months sufficient improvement had taken place for the patient to be discharged from that hospital. From that time until she was 2 years old and entered the Children's Hospital she had weathered attacks of measles, German measles and chicken pox, but had failed to gain weight satisfactorily. At 2 years she weighed 18 pounds, which is slightly under the normal weight for an infant of 1 year.

Physical examination showed an undernourished infant of good color. Percussion over the left chest posteriorly revealed dullness below the third rib and from the midline to the posterior axillary line. Anteriorly the percussion note was tympanitic. Breath sounds on the left were distant and only vaguely heard. The percussion note over the right chest was hyperresonant, but the breath sounds were normal and no rales were heard. The borders of the heart were difficult to define by percussion. The apex impulse could not be felt. The heart sounds were of normal rhythm but were distant. The abdomen was flat or perhaps a little scaphoid in appearance. The liver edge was 1.5 cm. below the costal border in the nipple line. The spleen was not palpable. No tenderness, muscular spasm or masses were felt.

Fluoroscopic examination showed the esophagus dis-

placed slightly to the right. The barium entered the stomach without difficulty. The whole of the stomach was inverted within the thoracic cavity, with the greater curvature lying superiorly and the pylorus lying inferiorly. Six hours after administration, all the barium was in the colon. The cecum and ascending colon were in the left side of the chest, with the appendix visualized just lateral to the heart. The findings were those of a left-sided diaphragmatic hernia, with apparently a portion of diaphragm remaining anteriorly and posteriorly.

Under Avertin and novocain anesthesia a small transverse incision was made in the left side of the neck 2.5 cm. above the clavicle. The phrenic nerve was crushed with a small hemostat, and the wound closed. Four days after the preliminary operation, the abdomen was opened under Avertin and ether anesthesia. A left rectus incision was made extending from the costal border to a point 2.5 cm. below the umbilicus. An opening 7.5 cm. long and 5 cm. wide in the left side of the diaphragm extended from the nipple line toward but did not connect with the esophageal opening. Above the diaphragmatic opening were found the whole of the stomach, the spleen, the splenic flexure, half the transverse colon and 10 or 12 cm. of the descending colon. These organs were very easily delivered from the thoracic cavity, since there were only a few light adhesions around the cardiac end of the stomach. The abdominal viscera presented the not very uncommon condition of an unrotated colon with a rudimentary mesenteric attachment. There was no oblique attachment to the posterior abdominal wall of the mesentery of the small bowel, and only a small area of attachment of the hepatic flexure of the colon. The cecum and ascending colon were lying loose in the epigastrium just under the hernial opening. An incision was made around the edge of the hernial opening through both the peritoneal and pleural layers. As soon as the pleura was opened and air entered the thoracic cavity, the sac was delivered with no difficulty and was completely excised. Through the opening in the diaphragm the lung was seen to be collapsed, and the heart next to it in the same cavity without any pericardial covering. The ventricles stood out plainly. The auricles were not seen, and it is not certain whether there was not a rudimentary pericardium, as found in some of the published autopsies. The hernial opening in the diaphragm was closed with a row of interrupted sutures of silk to the pleural layer, a row of mattress sutures of silk to the musculature of the diaphragm and a row of interrupted silk sutures to the peritoneal layer of the sac. The abdomen was closed in layers without drainage.

The first 24 hours after operation were somewhat stormy. The temperature rose to 104°F., the pulse to 180, and the respirations to 60. The blood pressure was 70 systolic, and 20 diastolic. By the end of another 24 hours the temperature had dropped to 101°F., the pulse to 130 and the respirations to 25. During this period there was a left-sided pneumothorax, with a 90 per cent collapse of the left lung; there was no displacement of the heart. From this time on, the convalescence progressed satisfactorily and uninterrupted. The patient was kept in the hospital longer than usual in order to make sure that there were no circulatory disturbances and that the lung was entirely expanded. She was discharged on the 26th day after operation. The wound was healed by first intention with a firm scar. The abdominal organs were in the abdominal cavity. The lung was completely expanded and there was no air or fluid in the pleural cavity.

The patient's general condition has been excellent since operation. She has gained weight, and has had no difficulty in breathing.

*This case, with a diaphragmatic hernia and absence of the pericardium, has been previously reported,⁴ but because of its unusual interest a note is inserted concerning it.

CASE 5 K C, a 6-week-old girl, entered the hospital on December 22, 1938, with a chief complaint of cyanosis since birth. At birth she weighed 6 pounds, 2 ounces. On the first day after delivery there were attacks of cyanosis and rapid breathing, particularly after the patient had been crying. It was found that these attacks could be controlled by placing her on her left side in an oxygen tent. Since that time cyanosis had appeared as often as three or four times a day, whereas on other occasions the color was normal for three or four days. The baby had taken its feedings well.

Physical examination showed that the thorax was symmetrical. The percussion note was resonant over the right side of the chest but dull over the left. The breath sounds were normal over the right lung but were completely absent over the left. Occasional gurgles could be heard on auscultation over the left side. Respirations were rapid. The heart was displaced to the right.

A ray examination of the chest showed the entire pleural cavity to be filled with loops of intestine, the left lung completely collapsed, the heart slightly displaced to the right and the right lung partially compressed.

Operation was performed on December 29, 1938, under drop ether anesthesia. A transverse incision was made in the neck above the left clavicle, and the phrenic nerve was crushed. The abdomen was opened through a left rectus incision, splitting the muscle from the costal margin almost to the pubis. The defect was found in the posterolateral portion of the diaphragm. The entire ileum, all the colon except the descending portion, and the spleen were in the left pleural cavity. These viscera were withdrawn through the diaphragmatic opening and pulled downward, some of them protruding through the abdominal wound. The edges of the diaphragmatic opening were freshened and sutured with mattress sutures of silk, supplemented by a continuous silk suture to the peritoneum. The abdominal wall was closed with some difficulty, owing to tension. The peritoneum and posterior rectus fascia could be approximated, although there was some tearing of these structures during the placement of the sutures. The anterior rectus fascia was brought together with interrupted silk sutures, and the skin was closed with sutures of interrupted silk.

The patient was given parenteral fluids and was kept in an oxygen tent for 3 days. The temperature rose to a peak of 102.4°F on the first postoperative day, but subsided to normal by the third day. The pulse rose to a peak of 160 and the respirations rose to as high as 70 on the 2nd postoperative day but both subsided to normal by the 5th day. There was no vomiting or distention. Feedings were begun after the 3rd day. The wound healed well, and the patient was discharged home on the 19th day.

A ray films of the chest on the afternoon of operation showed an extensive pneumothorax on the left with displacement of the heart and mediastinum to the right. The left lung was completely collapsed. No abdominal viscera were seen in the chest. The left lung spontaneously expanded and by the 10th postoperative day completely filled the left chest. A barium examination of the intestinal tract on the 19th day showed a slight deviation of the lower end of the esophagus to the right at the point of its passage through the diaphragm but there was no other evident abnormality. A film taken on May 6, 1939, showed the chest to be normal and the left diaphragm in the normal position.

The patient was last seen in December, 1939, at which time she was in excellent general physical condition.

CASE 6 J M, an 11-day-old boy, entered the hospital on February 12, 1939, for treatment of a diaphragmatic her-

nia. The labor had lasted 15 hours. During the delivery the mother's condition was good but the fetal condition was said to be poor. The baby was cyanotic at birth but was resuscitated with oxygen. The birth weight was 5 pounds 12 ounces. His respirations were shallow and rapid, cyanosis continued, and he was limp. He had to be kept continually in an oxygen tent during this 11-day stay at the maternity hospital. The cyanosis became severe, and the patient's condition critical if he was removed from the tent for more than a minute or two.

Inasmuch as the breath sounds were diminished over the entire chest, it was thought that there was a massive atelectasis of the lung. Because of generalized twitching, a lumbar puncture was performed, which showed clear fluid. On the 5th day, x-ray examination of the chest showed evidence of diaphragmatic hernia.

Physical examination was only cursory because of the critical condition of the patient, who was ashen gray. He had to be kept in an oxygen tent during the greater part of the examination. The respirations were shallow and were 87 per minute. The pulse was poor, and the patient appeared to be in a state of shock. There was occasional vomiting of small amounts of bile-stained fluid. Breath sounds were normal over the left chest, but were absent over the right. Peristaltic sounds could be heard over the right side of the thoracic cage.

A ray examination of the chest showed the entire right pleural cavity to be filled with abdominal viscera and the right lung completely collapsed. The heart was displaced to the left, and the left lung was compressed.

Operation was performed on February 14 under cyclopropane anesthesia. The right phrenic nerve was exposed above the clavicle and was crushed. The abdomen was opened with a right rectus muscle splitting incision running from the costal margin well down in the lower quadrant. There was a large defect in the posterior portion of the right diaphragm. Herniated into the right pleural cavity were a large right lobe of the liver, all the colon except the descending and the left half of the transverse portions, the distal half of the stomach and all the small intestine. Between the right and left halves of the liver there was a deep cleft into which the medial margin of the diaphragm fitted. The only way in which the contents of the right pleural cavity could be delivered was by first withdrawing the entire small intestine, then the large intestine and finally the right lobe of the liver. These viscera were displaced downward and to the left and the intestines were allowed to protrude through the abdominal wound. The edges of the diaphragmatic opening were freshened and brought together with interrupted mattress sutures of silk. The right lobe of the liver was then allowed to fall back against this line of sutures so as to buttress the diaphragm repair. It was found impossible to replace the intestines in the abdominal cavity, and to close the abdominal wound. Transverse incisions were made in each rectus muscle beginning from within the abdomen and cutting through all structures out to the subcutaneous tissues. This permitted closure of the subcutaneous fascia and skin of the abdominal wound. At the end of the procedure the patient's pulse and respirations were quite weak. He was given coramine and placed in an oxygen tent. His condition improved after a transfusion.

For 3 days after operation the patient was supported with parenteral fluids and was kept constantly in an oxygen tent. On the 1st postoperative day air was aspirated by inserting a needle into the right pleural cavity. There was no evidence of obstruction at any time. The skin sutures were removed on the 10th postoperative day. The patient's condition gradually improved so that he was discharged home at the end of 6 weeks.

X-ray examination on the afternoon of the operative day showed a pneumothorax on the right side and complete collapse of the lung. Subsequent films showed a gradual expansion of the lung, which was due to spontaneous absorption of air augmented by aspiration, and in about 10 days the right lung had completely filled its pleural cavity. Examinations of the gastrointestinal tract with barium 1 month after operation showed a normal stomach and intestines and no evidence of abdominal viscera in the thoracic cavity.

The patient was brought back to the hospital on June 24, at which time the incisional hernia of the abdominal wall was repaired. There was a satisfactory convalescence from this operation. When last seen, in December, 1939,

left phrenic nerve was exposed in the neck and was crushed. The abdomen was opened through a long left-rectus muscle-splitting incision running from the costal region well down into the left lower quadrant. Within the abdominal cavity were the distal third of the stomach and duodenum, the descending colon and the liver. Herniating into the left pleural cavity were the proximal two thirds of the stomach, the transverse and ascending colon, the jejunum, all the ileum and the spleen. The defect found in the posterolateral portion of the diaphragm was about 3 cm. long and 2 cm. wide. The abdominal viscera were readily withdrawn from the pleural cavity, no adhesions being encountered. The intestines were allowed to come out of the abdominal wound so as to give an ade-

TABLE 1. *Data from Successfully Treated Cases of Diaphragmatic Hernia.*

CASE No.	HOSPITAL No.	AGE	SEX	SITE OF HERNIA	MAJOR SYMPTOMS	OPERATIONS*	ANESTHESIA	RESULT
1	141149	4 wk.	F	Esophageal	Vomiting, cyanosis	Diaphragm repair	Ether	Slight recurrence, symptomatic cure.
2	192085	2 yr.	F	Left pleuro-peritoneal	Vomiting, cyanosis	Phrenic crush, diaphragm repair	Ether	Cure
3	199566	3 wk.	M	Left pleuro-peritoneal	Cyanosis	Diaphragm repair	Ether	Cure
4	224541	9 mo.	M	Esophageal	Vomiting	Diaphragm repair	Cyclopropane	Symptomatic cure
5	228119	6 wk.	F	Left pleuro-peritoneal	Cyanosis	Phrenic crush, diaphragm repair	Ether	Cure
6	229511	11 days	M	Right pleuro-peritoneal	Extreme cyanosis requiring oxygen	Phrenic crush, diaphragm repair; abdominal repair 4 mo. later.	1st operation, cyclopropane; 2nd, cyclopropane.	Cure
7	230878	18 mo.	M	Right pleuro-peritoneal	Vomiting, dyspnea	Phrenic crush, diaphragm repair	Cyclopropane	Cure
8	238818	40 hr.	M	Left pleuro-peritoneal	Cyanosis requiring oxygen	Phrenic crush, diaphragm repair; abdominal repair 8 days later.	1st operation, cyclopropane; 2nd, ether.	Cure
9	241377	48 hr.	M	Left pleuro-peritoneal	Cyanosis requiring oxygen	Phrenic crush, diaphragm repair; abdominal repair 4 days later.	1st operation, cyclopropane; 2nd, ether.	Cure

*A thoracic approach was employed in Case 4, an abdominal approach in all other cases.

the patient was very healthy, fat and well developed. He weighed 19 pounds and was in excellent general physical condition.

CASE 8. D. C., a 36-hour-old boy, entered the hospital December 26, 1939, because of repeated attacks of cyanosis since birth. After delivery he breathed spontaneously, but the color was poor; oxygen was given immediately and was continued for 1½ hours. When removal from the oxygen tent was attempted, the color grew worse. During the first day and a half there was usually some degree of cyanosis, which could be temporarily improved when the child was placed back in an oxygen tent. No feedings had been given. There had been no vomiting.

At physical examination the respirations were rapid. There was moderate cyanosis. The chest was symmetrical. Respiratory excursions were more marked on the right than on the left. There were a normal percussion note and normal breath sounds over the right lung. There was hyperresonance of the left chest, but no breath sounds could be heard. Auscultation over the area of the left lung revealed occasional loud creaks and some faint gurgling sounds, suggesting the presence of intestinal loops in the left pleural cavity. The heart appeared to be displaced toward the right.

X-ray examination of the chest showed the left pleural cavity to be completely filled with loops of intestine, the left lung compressed so as to be unrecognizable in the film, the heart displaced partly to the right and the right lung partially compressed.

On December 27, when the baby was 40 hours old, operation was performed under cyclopropane anesthesia. The

quate view of the under surface of the left diaphragm. The edges of the diaphragmatic opening were freshened, and the defect was easily closed with interrupted mattress sutures of silk, reinforced by a few interrupted silk stitches placed between the mattress sutures. On an attempt to force the intestines back into the abdominal cavity, it was found that the wound could not be closed in all its layers. It was impossible to approximate the peritoneum, the rectus muscle or the anterior rectus fascia. It was therefore decided to close only the subcutaneous fat and skin, which could be brought together rather easily. The subcutaneous fat was closed with a continuous silk suture, and the skin edges were approximated with end-on interrupted silk mattress stitches.

Following operation one transfusion of blood was given. The patient was placed in an oxygen tent. Respirations rose as high as 90 during the 1st postoperative day, but gradually fell to 40 by the 4th day. There was some fever for 3 days, after which the temperature remained normal. In order to avoid abdominal distention, the oral intake of fluid and milk was limited, and fluid requirements were fulfilled with the use of parenteral fluids and the administration of fluids by rectum. On the 7th day the skin sutures were removed and on the morning of the 8th day it was found that evisceration through the abdominal wound was beginning. Under drop ether narcosis the presenting loops of bowel were replaced in the abdominal cavity, and the abdominal wound closed with running catgut to the peritoneum and muscle in addition to through-and-through sutures of silk, including all layers except the peritoneum. It was striking to find that, within

these 8 days since the first operation the abdominal wall had stretched sufficiently so that the wound edges could be readily approximated without tension

Following the secondary repair the patient did well. There was no evidence of an incisional hernia and the baby was discharged home in excellent condition on the 33rd day of life. In June, 1940, 6 months after operation the baby was found to be in excellent health, above the normal weight for his age and having no respiratory or digestive difficulty, with the diaphragm in normal position, and with a firm abdominal scar and no hernia.

Since Orr and Neff's² collection from the literature of 9 cases of diaphragmatic hernia successfully operated on in the first year of life, we have found 8 more successful cases. Donovan³ has been the largest contributor to these results with 4 satisfactory cases. Three of these were cured, one after a secondary operation for recurrence, but the fourth patient had a slight recurrence without untoward symptoms. Sixteen patients with congenital diaphragmatic hernia have been operated on at the Children's Hospital since 1930. Nine of these have recovered, 7 of them being under one year of age (Table 1). The youngest patient was operated on when forty hours old. Of the 7 deaths, 1 occurred 5 days after a phrenicectomy before the herniorrhaphy was attempted, and 1 four days after operation, probably from pneumonia. The remaining 5 deaths were probably due to one or a combination of the following factors: failure to provide proper fluid balance, lack of positive pressure anesthesia or too tight closure of the abdominal wall.

SUMMARY

The time to make the diagnosis of congenital diaphragmatic hernia is immediately after the baby is born. The time to attempt cure is within the first few days after birth or as soon thereafter as the patient can be taken to a hospital equipped to handle this type of case.

The policy of delaying operation until the infant is older is a hazardous one, and has been responsible for many deaths in the past.

One of the greatest problems of operating on these patients in early infancy has been that of finding sufficient room in the underdeveloped peritoneal cavity to receive the abdominal viscera. This problem has now been solved by the procedure here reported of closing only the abdominal skin, allowing the abdominal wall to stretch and then suturing the peritoneum and the rectus muscles at a second operation five or six days later.

In our series, 9 patients have been successfully operated on. The youngest of these was forty hours old.

300 Longwood Avenue

REFERENCES

1. Hedblom, C. A. Diaphragmatic hernia: a study of three hundred and seventy-eight cases in which operation was performed. *J. A. M. A.* 85:947-953, 1925.
2. Orr, T. C., and Neff, F. C. Diaphragmatic hernia in infancy: under one year of age treated by operation. *J. Thorac. Surg.* 5:434-440, 1936.
3. Donovan, E. J. Congenital diaphragmatic hernia. *Ann. Surg.* 108:3-4, 338-348, 1938.
4. Ladd, W. E. Congenital absence of the pericardium: with report of a case. *New Eng. J. Med.* 214:183-18, 1936.

INDICATIONS FOR GASTROSCOPY*

EDWARD B. BENEDICT, M.D.[†]

BOSTON

GASTROSCOPY with the flexible gastroscope has now become a generally accepted method of examining the stomach. It gives information regarding the gastric mucosa that is not obtainable by any other procedure. It is particularly important in studying color and detail. Since no other examination gives such information, it is obvious that gastroscopy supplements but does not replace other methods of examination. It is an additional diagnostic procedure of very great value and should be, as Schindler¹ has pointed out, "a routine method of the gastroenterologist, just as cystoscopy is a routine method of the urologist."

The technic of gastroscopy has been fully described,¹⁻³ but it may not be amiss to review its essential points, especially those dealing with its simplification. After sufficient experience has been attained, the procedure may be carried out in the

office or the outpatient department with the aid of one assistant. X-ray examination of the esophagus and stomach is always carried out before gastroscopy to exclude any esophageal lesion that might contraindicate the blind passage of the gastroscope. This should be done several days in advance so that no barium will remain clinging to the gastric mucosa. The patient should report with an empty stomach, ½ gr. of codeine and 1/150 gr. of atropine are given subcutaneously, and he is instructed to relax for one half to three quarters of an hour. Anesthesia of the throat is then obtained by a 2 per cent Pontocaine gargle. The gagging is done twice, it easily produces satisfactory local anesthesia and eliminates the necessity of any elaborate anesthetizing methods. If there is a history of vomiting or any evidence of pyloric obstruction, the stomach is then emptied of secretions, either by aspirating through a small duodenal tube or by gravity drainage through a

*From the Massachusetts General Hospital.
[†]Assistant in surgery, Harvard Medical School; assistant surgeon, Massachusetts General Hospital.

large stomach tube with the patient in the Trendelenburg position. For this procedure Schindler's special table is very convenient and satisfactory. The best position for gastroscopy is with the patient lying on the left side with the left elbow under the chest, the right arm hanging loosely over the edge of the table and the head extended on small, firm pillows. It has been my experience that patients relax more completely with the head securely supported on pillows than in the hands of an untrained assistant. Since a trained assistant is frequently unavailable, this simplification of the technic has permitted greater independence in the scheduling of cases, and has also given the examiner greater confidence in the handling of difficult patients.

The actual introduction and passage of the gastroscope present no particular problem if proper attention has been given to the preliminary details, especially the correct position on the examining table. With the right hand holding the rigid part of the instrument and the left hand supporting the tip as it enters the patient's mouth, the tongue is depressed by the first two fingers of the left hand, the tip advanced in the midline to the posterior pharynx, the esophageal orifice found and the instrument introduced into the stomach. Much has been written about the advisability of rapid introduction of the gastroscope to avoid spasm, but in my opinion too rapid passage may be dangerous.

The first indication for gastroscopy is gastritis, or suspected gastritis, for it is in the observation of the finer changes in the gastric mucosa that the procedure has its greatest field of usefulness. Since gastritis is the commonest disease of the stomach, the value of gastroscopy is self-evident.

CASE REPORTS

CASE 1. J. E. G. (M. G. H. U28421), a 51-year-old white, married American patternmaker, first came to the Out Patient Department in 1925 with a story of gas, indigestion and pain not related to meals. Gastrointestinal x-ray examination at that time showed no definite evidence of organic disease of the esophagus, stomach or duodenum. An additional history obtained at this time showed that the patient took whiskey once a week and chewed tobacco almost continually. Worry was a factor in increasing the symptoms.

Gastroscopy performed on June 7, 1934, showed the pylorus to be normal. Normal rugae were almost entirely absent and were replaced by elevations and depressions of an irregular character. The mucosa was deeper red than usual. The findings were those of hypertrophic gastritis. The patient was placed on a rigid routine, with a six-meal bland diet and complete elimination of alcohol and tobacco. On this regimen he showed moderate improvement. X-ray examination in October, 1936, was again negative. On November 5 gastroscopy was again performed. The rugae were small and presented a beaded appearance throughout the body and fundus of the stomach. The mucosa also was generally verrucous and showed a blotchy reddening. The findings were those of

a definite hypertrophic gastritis. At this time it was found that the patient had no free hydrochloric acid in the fasting contents. Dilute hydrochloric acid was given as medication, and the patient was advised to eat liver three times a week. Two months later he was again seen in the Gastrointestinal Clinic; he had gained weight and was feeling better than he had been for 5 years. When last seen in the clinic in September, 1937, he had continued to gain weight and was symptom-free on the regimen described above.

Comment. Gastroscopic examination of this patient, who presented a vague history and negative x-ray examination, permitted a positive diagnosis of hypertrophic gastritis and enabled us to treat intelligently this patient's condition, with notable success. We are accumulating some evidence in this clinic that liver is of benefit in the treatment of gastritis, the rationale of such treatment being the improvement in the atrophic gastritis of pernicious anemia following liver therapy as previously reported by Jones, Benedict and Hampton.³

A second very important indication for gastroscopy is unexplained gastrointestinal hemorrhage. A gastroscopic study of patients with hemorrhage from gastritis has recently been reported by Benedict.⁴ The following case is a good example.

CASE 2. J. G. L. (B. M. U78062), a 69-year-old married American housewife, first entered the Baker Memorial Hospital in September, 1937, complaining of attacks of epigastric pain with nausea and vomiting. These attacks had come on at irregular intervals for a period of fifteen years. The patient had been repeatedly examined at various hospitals, with negative results. For several weeks prior to admission she had passed very dark stools.

The red-cell count on admission was 3,000,000. X-ray examination showed the esophagus to be normal. There was a diverticulum of the posterior wall of the fundus of the stomach near the esophageal orifice. The stomach, pyloric valve and duodenum were otherwise normal except for a second diverticulum off the beginning of the second portion of the duodenum. No cause, however, was found for the gastrointestinal bleeding. A barium enema was negative. A Graham test was also negative. X-ray examination of the upper gastrointestinal tract was repeated on October 14 and again failed to demonstrate any cause for hemorrhage. Gastroscopy performed on October 27 showed the pylorus to be normal, the antrum normal and peristalsis normal. Just proximal to the muscular sphincter antri on the lesser curvature was an erosion 1 mm. deep and 3 mm. in diameter with slightly reddened margins. On the greater curvature there was a definite red streaking of the crest of one fold. There was an area of superficial reddening on the posterior wall in the body of the stomach. The mucosa of the posterior wall in the upper part of the body was markedly verrucous and showed a blotchy reddening. Increase of mucus near the cardiac orifice prevented a satisfactory view of the opening of the diverticulum. Toward the posterior wall, however, a glimpse was obtained of a dark, circular orifice that was probably the narrow mouth of the diverticulum. There was no marked reddening around it. The findings were those of superficial and hypertrophic gastritis with erosions. Continuation of a six-meal bland diet with liver and iron was advised. This recommendation was followed, and the patient has remained well for 2 years.

Comment. This case is typical of many cases of gastric hemorrhage, in which all other methods of examination have been entirely negative, but gastroscopy has revealed

the correct diagnosis and enabled the institution of rational therapy

It should be emphasized that gastroscopy should be performed within a few days of the hemorrhage, for the delay of even a week will not infrequently mean healing of the gastric mucosa and a false negative examination. No untoward results have been observed from early examination after hemorrhage. It is amazing how rapidly erosions and superficial ulcerations heal and leave no scar whatever. Even true peptic ulcers may heal very rapidly under ideal conditions. In the same way erosions and ulcerations may develop with great rapidity, with resultant almost daily change in the gastroscopic picture. The dictum is, therefore "Perform gastroscopy early."

A third important indication for gastroscopy concerns cases of so called "gastric neurosis." That a patient may appear neurotic and x-ray examination may fail to reveal any basis for gastric symptoms does not necessarily mean that no basis exists. Chronic gastritis may be the cause of the symptomatology in such a case and may, in fact, be a contributing factor in the nervous condition of the patient, if a diagnosis of neurosis is justifiable. Chronic gastritis may explain the whole picture, or there may be an additional neurotic element. The following is a case in point.

CASE 3 M E McN (M G H U5425) a 39 year old, married Canadian housewife, first entered the hospital in February, 1933, complaining of almost constant epigastric gnawing and distress, coming on 1 or 2 hours after meals for the last 4 years. There had been some improvement on a six meal bland diet. A gastrointestinal x-ray exam was negative. The patient was a very nervous woman, with multiple complaints and many worries. A complicating factor was a positive diagnosis of tabes, which made a diagnosis of gastric crises very possible. Since it was necessary to perform a hysterectomy and bilateral salpingo-oophorectomy for pelvic inflammation in 1932, the condition was also somewhat complicated by menopausal symptoms. Gastrointestinal symptoms, however, persisted, with gurgling and distress in the epigastrium in 1934, bloating and anorexia in 1935 and gastric gnawing and epigastric pain in 1936. In October, 1936, gastrointestinal x-ray examination was again negative.

Gastroscopy on October 23, 1936, showed the pylorus to be normal, the antrum normal and peristalsis normal. The rugae were not enlarged or tortuous. In the upper part of the stomach on the greater curvature and posterior wall there was very marked reddening with a somewhat blotchy appearance. There were also some verrucous elevations in the mucosa of this region. The findings were those of hypertrophic gastritis in the upper part of the stomach. The patient was again put on a six meal bland diet and advised to take liver four times a week. There was some improvement. In October, 1938, she was again seen in the Gastrointestinal Clinic. She had been adhering more closely to the diet for the last 2 years and had been feeling quite well. Her appetite had improved. At that time she was taking cod liver oil, yeast and iron. During the last 2 weeks she had had occasional attacks of nausea and vomiting, with pain in the left upper quadrant and along the left costal margin. Further x-ray

study and gastroscopy were advised, but have not as yet been carried out.

Comment This patient's symptomatology might well have been considered due to tabes, artificial menopause and neurosis, but gastroscopy demonstrated a lesion in the stomach as a basis for her symptoms, and treatment of that condition resulted in some improvement. That there has not been complete relief is not surprising when the complicating factors in this case are considered, and when we realize that hypertrophic gastritis is a chronic disease that is frequently difficult to treat.

A fourth use for gastroscopy is in cases where x-ray examination is negative but gastrointestinal symptoms persist. Such a case is the following.

CASE 4 M I B (M G H U83951), a 41 year-old, white, married American housewife, entered the hospital in March, 1934, with a 12 year history of gas, epigastric pain, vomiting and tarry stools. X-ray examination had been performed in February, 1933, and had shown a pressure defect on the lesser curvature side of the duodenal cap, probably from the gall bladder. A Graham test done at this time showed no normal filling of the gall bladder, but this was repeated in 1934, when the gall bladder filled normally and the test was considered negative. X-ray examination of the gastrointestinal tract on this admission showed no evidence of organic disease of the esophagus, stomach or duodenum.

Because of the persistence of symptoms, however, gastroscopy was performed on March 22, 1934, and showed 2 erosions of the anterior wall, where the mucosa was granular and nodular. One of the folds of the greater curvature showed a definite clubbing at its crest and an erosion about 2 to 3 mm in diameter. On the posterior wall in the fundus of the stomach the mucosa appeared pitted, with many marked irregular elevations and depressions. The appearance was that of hypertrophic gastritis with erosions. The patient was discharged on a bland diet with belladonna, and was definitely improved 2 months later. Three years later, however, after having reverted to eating only 3 times a day and to smoking cigarettes, she had a recurrence of gas, nausea, occasional vomiting and distress. Further x-ray and gastroscopic examinations were advised but were not carried out.

Comment This patient's gastrointestinal symptoms were not explained until gastroscopy demonstrated hypertrophic gastritis with erosions. Rational treatment in this case resulted in improvement, but the patient failed to co-operate for a sufficiently long period of time.

Another important indication for gastroscopy concerns cases in which x-ray examination is inconclusive.

CASE 5 F S T (B M U127931), a 57 year-old, single department manager, was referred for gastroscopy in June, 1938. The patient gave a 2 year history of indigestion and anorexia. X-ray examination on May 12, 1938, showed the esophagus to be normal. The stomach was unusually large and contained a large amount of retained secretion and food. The prepyloric region was not well visualized. The barium passed only in small amounts to this region. The nature of the obstruction in the region of the pylorus could not be definitely demonstrated, but seemed suggestive of ulcer. Re-examination was requested. X-ray examination on May 14 showed a large amount of retained secretion. The barium was very dilute. There was still a large amount of food, but the gastric folds were seen to be considerably thickened, particularly along the lesser curvature and the incisura angularis. No barium passed into the duodenum. Re-

suggested after gastric lavage to determine the cause of the obstruction in the region of the pylorus.

Two days later gastroscopy was performed. In spite of gastric lavage on the ward, preliminary drainage of the stomach with the large stomach tube and the patient in the Trendelenburg position yielded 75 cc. of cloudy, bile-stained secretion. The stomach was again lavaged on the operating table. This secretion contained no free hydrochloric acid. On the lesser curvature near the pylorus was an ulceration about 5 by 3 cm. in size with ragged, nodular, proliferating margins and a dirty-gray base. The ulceration was shallow. The complete pyloric sphincter could not be seen beyond the ulceration, although part of it was visible and gave the impression of being 1 to 2 cm. beyond the ulcer. Higher up in the body of the stomach toward the posterior wall and the lesser curvature there were several smaller nodules of a reddish color, which probably represented a continuation of the malignant process, but might have been due to hypertrophic gastritis. The findings indicated a fairly extensive carcinoma of the stomach, involving the lesser curvature. Because of the extent of the disease and the lack of obstructive symptoms a laparotomy was not advised. Peritoneoscopy^{5, 6} was performed on May 23 and showed the liver to be studded throughout with yellowish nodules, varying in size from 3 to 4 mm. to 2 to 3 cm. in diameter, and having the characteristic appearance of carcinoma. A biopsy specimen of the liver at the time of peritoneoscopy showed metastatic carcinoma. X-ray examination on June 16 confirmed the diagnosis of carcinoma, showing a large, dishlike ulceration in the middle of the lesser curvature. X-ray treatment was given, with moderate improvement, but when last heard from the patient was failing rapidly.

Comment. In this case x-ray examination was incomplete on 2 occasions owing to the large amount of retained food and secretion in the stomach. X-ray examination after gastric lavage, as suggested, was not done. Gastroscopic examination resulted in a positive diagnosis of extensive carcinoma. That this was inoperable was demonstrated by peritoneoscopy, at which time a peritoneoscopic biopsy specimen from the liver showed metastatic carcinoma.

Gastroscopy is of value in many cases of gastric ulcer in determining the appearance and location of the lesion and following the healing process. The following is a case in point:

CASE 6. S. M. D. (M. G. H. U1997), a 34-year-old housewife, came to the hospital in February, 1938, with a history of epigastric pain, nausea, vomiting and hematemesis. The history was of 14 years' duration, dating back to 1924, at which time x-ray examination showed a duodenal ulcer, and symptoms were relieved by a bland diet. There had been recurring attacks at intervals up to the present entry. X-ray examination in 1936 showed hypertrophy of the gastric rugae, a large ulcer of the lesser curvature of the stomach and a duodenal ulcer. Gastroscopy was suggested by the X-ray Department at this time but was not performed. Gastrointestinal x-ray examination at the present admission showed active gastric ulcer, marked hypertrophic gastritis and an inactive duodenal ulcer.

Gastroscopy was performed on May 26, 1938, and was reported as follows:

The pylorus is well seen and appears normal. Peristalsis and the antrum are normal. Just at the musculus sphincter antri on the lesser curvature there are 2 ulcers, each about 1.0 to 1.5 cm. in diameter. Both are very shallow and show a clean-gray base with pale

margins. They appear to be healing and inactive. The mucosa surrounding the 2 ulcers is essentially normal. There is no evidence of hypertrophic gastritis, although there is some increased reddening, indicating a slight degree of superficial gastritis.

On a rigid medical regimen the patient made an excellent recovery with gain in weight, and was doing very well when last seen 6 months after gastroscopy.

Comment. This case brings up a number of interesting features. In the first place, gastroscopy gave the added information that there was more than one gastric ulcer. This of course is of very great importance with regard to the treatment and prognosis, for a patient with multiple ulcers in the stomach as well as in the duodenum must have a marked tendency toward ulcer formation, and should consequently be particularly careful as to treatment. In the second place, the gastroscopic description of a shallow ulcer with a clean base indicated that both lesions were benign and were healing satisfactorily. In the third place, gastroscopy gave information with regard to the gastric mucosa, which indicated that the gastritis was very slight and superficial, whereas it was described two months previously, following x-ray study, as a very severe hypertrophic gastritis. There can be no question that gastritis may improve very markedly in two months, but that a severe hypertrophic gastritis may revert in that period of time to a slight superficial condition seems rather unlikely, and makes one question the accuracy of the roentgenological diagnosis. Roentgenologists are the first to admit the superiority of gastroscopy over roentgenology in the diagnosis of gastritis.^{7, 8} Everyone admits that a negative x-ray examination does not exclude gastritis. Some significance, however, should usually be attached to a positive x-ray diagnosis of gastritis, although it is universally agreed that the roentgenologist cannot classify the types of gastritis or satisfactorily study the progress of the disease.

In cases of duodenal ulcer, gastroscopy not infrequently gives important information regarding the gastric mucosa. It is, of course, impossible to see beyond the pylorus by gastroscopy, and consequently the ulcers of the duodenum cannot be studied. There is often, however, a chronic gastritis associated with duodenal ulcer. After the ulcer is apparently healed the gastritis may persist and cause symptoms. If surgical treatment is contemplated in a case of ulcer of the duodenum, it is important for the surgeon to know the condition of the gastric mucosa. If this is normal, a simple gastroenterostomy or pyloroplasty may be indicated, but if a severe gastritis is present it may be necessary to do a subtotal gastric resection, removing not only the duodenal ulcer but also the diseased gastric mucosa. The following case illustrates this point.

CASE 7. L. A. (M. G. H. U18812), a 29-year-old, single American electrician, was first admitted on September 6, 1932, with a complaint of intermittent epigastric pain. The x-ray picture was not characteristic but could have been due to duodenal ulcer. On medical treatment the patient did very well for 4 years.

The second admission was on May 28, 1937, the patient having had recurrence of symptoms with loss of weight. X-ray examination showed an active duodenal ulcer with

moderate pyloric obstruction. Careful medical treatment was again given.

At the third admission, November 13, 1937, there was recurrence of epigastric pain with localized tenderness and nausea but no vomiting. A x-ray examination again showed active duodenal ulcer. Because of the poor response to medical treatment gastroscopy was advised and showed marked hypertrophic gastritis. Because of high acidity and extensive gastritis, partial gastrectomy with removal of the ulcer was advised.

At the fourth admission, December 29, 1937, all consultants agreed that radical operation was indicated. This was performed on January 5, 1938. Gastric resection with posterior Polya anastomosis was performed. The lower half of the stomach was resected. The pathological report showed healing duodenal ulcer with chronic gastritis.

The fifth admission was on November 19, 1938, the patient having remained symptom free for 11 months following gastric resection. He was then suddenly seized with generalized crampy abdominal pain causing him to double up. The pain quickly localized in the right lower quadrant. He vomited 3 times and had a chill. At operation a volvulus of the small intestine was reduced with lysis of adhesions. The patient was discharged relieved on December 8.

Comment. This is the history of a patient suffering from duodenal ulcer and chronic gastritis. Surgery was delayed for many years in the hope of obtaining cure on a medical regimen, but no relief was obtained. Gastroscopy showed the extent and severity of the gastritis, which had not hitherto been suspected, and at once gave the indication for radical surgery. The pathological report confirmed the x-ray diagnosis of duodenal ulcer and the gastroscopic diagnosis of chronic gastritis, showing, however, only a small healing duodenal ulcer. The persistent symptoms were quite likely due in large part to the very marked degree of hypertrophic gastritis associated with the duodenal ulcer. So far as his stomach is concerned, this patient has been symptom free for a period of 1 year since gastric resection.

Similarly in a recent case of duodenal ulcer it was observed that while the ulcer was healing, as shown by x-ray examination, the patient's symptoms were getting progressively worse. Gastroscopy showed a marked degree of chronic hypertrophic gastritis with three superficial ulcerations in the gastric mucosa. It may, therefore, reasonably be concluded that the gastritis and the gastric ulcerations were the cause of his persistent symptoms. From this and other similar observations it follows that no gastrointestinal study is complete without gastroscopic examination.

The importance of gastroscopy in differentiating benign and cancerous lesions has been previously emphasized.¹⁰ Schindler believes that the presence of the circulating blood makes it easier to differentiate cancer and ulcer in the living tissue than in the pathological specimen, even immediately after resection. Most clinicians and pathologists will probably not agree with this, and only gastroscopic observations in a large series of cases will prove or disprove the point. There is no doubt, however, that in certain cases gastroscopy

can give valuable information in the differentiation of benign and malignant lesions of the stomach. Technical difficulties such as high position of the stomach or obesity may interfere with satisfactory x-ray examination. Slight rigidity of the gastric wall may give the roentgenologist cause for grave concern, and when there is any doubt, gastroscopy should be performed. The following case exemplifies the assistance given by gastroscopy.

CASE 8. W S B (B M U12596) a 59-year-old, married American engineer, first entered the hospital on May 24, 1938, with the complaint of intermittent attacks of epigastric pain and indigestion of 30 years duration. The attacks lasted for 2 to 6 weeks at a time, with severe gnawing epigastric pain associated with gaseous eructations and flatulence. Repeated gastrointestinal x-ray examinations had been negative. A cholecystectomy had been performed at another hospital 29 years previously, without relief.

X-ray examination showed a flat, plateau like carcinoma of the lesser curvature of the stomach, which was producing obstruction. Gastroscopy showed an ulceration about 2 cm in diameter, with sharp red margins and a clean white base, about 2 or 3 cm proximal to the pylorus. The lesion looked very shallow. The surrounding tissue did not appear indurated. Peristaltic waves seemed to pass over this region. The depth of the ulcer crater did not appear to be more than 2 mm. There was moderate reddening of the mucosa in this region but no evidence of hypertrophic gastritis or of a nodular proliferating lesion. There was a small, red erosion on the crest of a fold of the greater curvature in the body of the stomach. The findings were consistent with a benign ulcer of the lesser curvature near the pylorus. After gastroscopy the x-ray films were checked and found to coincide with the gastroscopic findings. There had been an error in x-ray interpretation.

After 3 weeks of hospitalization on a strict ulcer diet the patient improved markedly. Gastroscopy was then repeated. It showed the lesion to be very much smaller and to have the characteristic appearance of a benign healing gastric ulcer. X-ray examination was also repeated and showed a healing prepyloric ulcer that was still producing incomplete obstruction.

The patient was discharged on the same day very much improved. He has been entirely symptom free for the last year and a half, feeling better than for many years and working under high pressure.

Comment. The above case illustrates the additional information obtained by a direct view of the lesion through the gastroscope. Until the time of gastroscopy there was a strong possibility of cancer of the stomach, with the certainty of surgical intervention unless that diagnosis was modified. Gastroscopy, however, showed the lesion to be benign, and this has been borne out by the subsequent course of the patient, with complete relief on a strict ulcer regimen.

In certain cases of malignant disease of the stomach gastroscopy is helpful in determining the extent and operability of the lesion.

CASE 9. F D F (M G H 333523), a 57-year-old single American farmer, entered the hospital on November 22, 1933, complaining of indigestion of 6 months duration gradually getting worse and associated with recurrent vomiting for the last 3 weeks. Physical examination

showed a sense of resistance in the epigastrium, but no definite mass was palpable.

X-ray examination three months before admission was reported as follows:

The stomach is atonic, and medium in position. Ten per cent residue is present, together with a considerable amount of fluid. The antrum is definitely narrowed. The pyloric valve is constantly spastic. There is a prominent persistent incisura on the greater curvature 5 cm. from the pyloric valve. The lesser curvature is quite straight. Sluggish peristalsis is seen to be present over the stomach. The duodenal cap is never well filled, owing to spasm of the pylorus. The appearance suggests a lesion on the lesser curvature, which is not demonstrated at this examination. Recommend examination of the patient without a motor meal.

A week later the report read:

Re-examination shows the same process described previously. This has the appearance of carcinoma of the greater curvature of the stomach about 2.5 cm. from the pylorus.

Operation was advised at that time, but the patient refused.

X-ray examination repeated on admission was reported as follows:

Re-examination with stomach tube confirms the previous findings. There is fixation of the lower 8 cm. of the stomach with deformity of the greater curvature. There is definite evidence of obstruction. The lesion has shown very little gross change in 3 months.

Three days later gastroscopic examination was done and showed a very extensive lesion of the stomach. The report was as follows:

There is considerable barium in the middle portion of the greater curvature, apparently caught in the folds of the lesion. The lesion itself appears very extensive, probably involving most of the greater curvature and some of both the anterior and posterior walls. The lesser curvature is not well seen. No normal rugae are seen. The appearance is that of extensive ulcerating carcinoma.

From this report it was evident that the disease was very advanced. Exploratory operation was undertaken, however, on November 28, and showed an extensive carcinomatosis, primary in the stomach, with metastatic disease scattered throughout the peritoneal cavity. No resection or palliative procedure was undertaken. Biopsy from one of the metastatic lesions showed carcinoma.

Comment. Gastroscopy in this case showed a much more extensive carcinoma of the stomach than had previously been suspected.

In polyposis of the stomach, gastroscopy frequently gives essential information regarding the size of the lesion, its basal attachment and the general appearance of the surface. Large lesions are almost surely malignant. Lesions with a broad base are likely to be so, and as Benedict and Allen¹⁰ have previously reported, there is likelihood that any adenomatous polyp will become malignant. The gastroscopic appearance of the lesion is therefore of great importance in determining the operative procedure. The following case not only demonstrates the value of gastroscopy in polyp of the stomach but also illustrates another indication for it, namely, observation of the changes in the gastric

mucosa in pernicious anemia before and after liver treatment.

CASE 10. E. D. S. (M. G. H. U6073), a 67-year-old Canadian street-railway operator, entered the hospital July 3, 1934, complaining of dyspnea and general weakness of 6 months' duration. For the last month nausea and vomiting had been prominent symptoms. Numbness of the fingers and toes had also been noted.

Physical examination showed a fairly well-developed man with a slight icteric tint to the skin. There was slight tenderness in the mid-epigastrium but no palpable mass. The red blood count was 1,400,000, and the hemoglobin 45 per cent. The smear showed marked anisocytosis, moderate poikilocytosis, large macrocytes, microcytes, and reduced platelets.

X-ray examination on June 26, 1934, just prior to admission, was reported as follows:

Examination of the esophagus is negative. There is an irregular filling defect, showing evidence of craters involving the lower half of the stomach. The duodenum shows a constant deformity that appears extrinsic. The findings are those of carcinoma involving the lower half of the stomach, with an extrinsic compression defect on the duodenum.

On July 5 re-examination by x-ray confirmed the previous observation. The same large defect in the pyloric end of the stomach was noted.

Gastroscopy performed on the following day was reported as follows:

The entire mucosa is very pale and thin, so that numerous small blood vessels can be seen very well. Normal rugae are almost entirely absent. On the lesser curvature and posterior wall in the antrum of the stomach there is a rounded elevated red lesion, which is fairly smooth in contour and which is attached to the mucous membrane by a broad base. This lesion is about 7 or 8 cm. in diameter and may well be a large benign polyp, but of course there is a very good chance of its now being malignant. The mucosa is typical of the atrophy seen in pernicious anemia. The association of pernicious anemia and polyp of the stomach is so common as to make me believe that the tumor in this case probably arose as an adenomatous polyp.

After liver therapy and transfusion, operation was undertaken on August 7. The following is the operative note:

A 15-cm. epigastric incision was made. The stomach was delivered without difficulty. In it could be felt a definite polyp. The stomach was opened and arising from the posterior wall, about one third of the way from the pylorus, was a long, tongue-like polyp about 15 cm. in length and ulcerated in two places. It was excised with a wide margin around the base, not making a hole clear through the posterior wall. Immediate examination of the specimen showed no evidence of malignancy. The stomach was closed in three layers with fine catgut.

The pathological report was: "Gastric polyp; no evidence of malignancy."

Following operation the patient made an uneventful convalescence, gained weight and strength, and was able to return to work. Through a misunderstanding he was careless about liver therapy and consequently suffered a relapse 3 months after discharge, but was quickly restored to health after proper treatment was instituted.

Gastroscopy 5 months after operation was reported as follows

The mucosa presents a very different appearance from that on previous examination. The color is nowhere very pale though moderately so in some places. In other areas the color is approximately normal, gradually paling off and presenting a somewhat blotchy appearance. Rugae are present along the greater curvature and appear somewhat irregular, but of nearly normal size. There is no evidence of a recurrence of the polyp, but near the antrum some areas show a pseudopolypoid arrangement. I believe there is a chronic gastritis, in a transitional stage perhaps from the atrophic variety seen in untreated pernicious anemia toward the verrucous or hypertrophic type. The findings indicate definite improvement.

Comment. This history records a case of benign gastric polyp associated with pernicious anemia. Gastroscopy revealed a smooth, elongated lesion suggestive of a benign polyp, although malignancy at the base of the lesion could not be excluded. At operation the lesion was demonstrated to be a finger-like benign polyp, which was locally excised with a wide margin. The pathological report showed the lesion to be benign. The association of benign polyp of the stomach with pernicious anemia is too well known to require any comment. The improvement in the gastric mucosa of pernicious anemia seen after liver therapy was first reported by Jones, Benedict and Hampton.³

The postoperative examination of the stomach by gastroscopy is of very great value. Many patients after gastroenterostomy or gastric resection continue to have symptoms, some mild and some severe. Some patients complain of the same symptoms that were present before the operation, but many present a vague symptomatology that is often unexplained by the usual studies. Gastroscopy in such cases may demonstrate severe postoperative gastritis.

CASE 11 J E K (M G H 30620), a 29-year-old, single American chauffeur, was admitted to the hospital June 9, 1934, because of epigastric discomfort and weakness of 5 days' duration. A posterior gastroenterostomy had been performed 13 years previously at another hospital when the patient was only 16 years old, because of symptoms thought to be due to a duodenal ulcer. Following operation the patient had a return of his original symptoms, accompanied by hematemesis and melena. No duodenal ulcer was demonstrable by x-ray examination. Because of hemorrhage, exploratory laparotomy was performed, with pylorotomy. No duodenal ulcer was demonstrable. The gastroenterostomy stoma appeared normal.

The second admission was on June 8, 1935, because of tarry stools. X-ray examination showed a well-functioning anastomosis, dilatation of the anastomosed jejunum and marked swelling of the gastric rugae.

The third admission was on November 27, 1935, because of severe hematemesis and melena. The red-cell count was 1,500,000. Gastroscopy at this time showed what appeared to be old blood in the stomach, with reddening and erosions of the mucosa. It was believed that much of the hemorrhage came from severe postoperative gastritis. X-ray examination showed thickened mucosal folds with deep crypts between them, simulating ulcer craters. No definite ulcer could be demonstrated.

The fourth admission was on March 18, 1937, because of severe recurrent hematemesis after considerable alcohol intake. The red cell count was 1,100,000. X-ray examination showed marked swelling of the rugae about the stoma but no definite ulcer. Gastroscopy was not done.

The fifth admission was on September 14, 1937, because of the recurrence of severe hematemesis, with the red-cell count 1,800,000. X-ray examination again showed hypertrophy of the gastric rugae but no definite ulcer and no evidence of esophageal varices. Gastroscopy showed evidence of a marked hypertrophic gastritis, that is, increased reddening and a verrucous appearance of the mucosa, with one erosion.

The sixth admission was on January 16, 1938, because of melena. The red cell count was 3,000,000. X-ray examination and gastroscopy were not done.

The seventh admission was on May 19, 1938, because of the passage of a large tarry stool. The red-cell count was 3,000,000. Gastroscopy showed a marked improvement in the gastric mucosa. X-ray examination showed no ulcer and no swelling of the mucosa.

The eighth admission was on January 9, 1940, because of recurrent hematemesis. The red cell count was 1,900,000. X-ray examination again showed no ulcer, but there was a widening of the gastric rugae. Gastroscopy showed increased reddening of the mucosa, with exudate in the valleys between the folds. There was old blood in the stomach, a cobblestone appearance on the posterior wall and several areas of erosion and ulceration. The findings indicated superficial and hypertrophic gastritis with erosions. Gastric resection was advised but refused.

The ninth and final admission was on August 27, 1940. During the 8 months since the previous admission the patient had been fairly comfortable until shortly before being admitted, when he passed a tarry stool. The red cell count was 3,600,000 but rose after transfusion to 5,000,000. At this time the patient agreed to subtotal gastric resection, which was performed. The convalescence was uneventful. Pathological examination showed a very red and injected gastric mucosa with prominent rugae. One cubic millimeter from the posterior gastroenterostomy stoma there was a small punched-out erosion 4 mm in diameter. The pathological diagnosis was chronic gastritis.

Comment. This case is one of a young man repeatedly admitted to the wards of the hospital for very severe hemorrhage. At no time was it possible to demonstrate any thing more than severe gastritis as the cause of hemorrhage. Gastroscopy repeatedly showed the degree of gastritis present—very severe with multiple erosions at some examinations but with nearly normal mucosa at others. Because of the many recurrences of severe hematemesis, subtotal gastrectomy was performed. The pathological report of chronic gastritis with erosion confirmed the gastroscopic and x-ray findings. No ulcer was present. Severe hemorrhage from gastritis is one of the few indications for resection in this disease.

This case demonstrates that severe postoperative gastritis is a very real entity and may be the cause of severe symptoms. The progress of the disease is best followed by repeated gastroscopic examinations.

Another indication for gastroscopy is the presence of a foreign body in the stomach. In known cases the open tube gastroscope¹¹ has been used for many years in removing such bodies. The new flexible gastroscope, however, may be useful in differentiating a polyp in the stomach from a

foreign body, as shown by the following unusual case.

CASE 12. E. D. (M. G. H. U29583), a 43-year-old, married, American housewife, first entered the hospital on April 24, 1937, because of epigastric distress of 2 years' duration. A diagnosis of peptic ulcer had been made 20 years previously, at which time she had obtained relief by following a diet. X-ray examination showed multiple extensive defects in the lower two thirds of the stomach; these could not be moved on palpation but had the appearance of food. There was a definite lesion in the pylorus—probably ulcer. The report of a repeated x-ray was as follows:

There is narrowing of the prepyloric region, with at least three grape-shaped defects in the prepyloric area. At least two of these defects can be moved away from this area and brought into the body of the stomach. The findings are those of a lesion in the prepyloric region. The defects described are present in spite of stomach lavage, and are identical with those seen at the previous examination. Their extreme mobility and the absence of a demonstrable pedicle are against a polyp, which, however, is still considered the most likely diagnosis. Recommend gastroscopy.

Gastroscopy was performed May 1, 1937. The report was as follows:

Just inside the cardiac orifice on the greater curvature a purplish-black, irregularly shaped object about 1 to 2 cm. in diameter is clearly visible and appears to lie free and movable in the stomach cavity. It is probably a foreign body. Just proximal to it is a second object of a yellow color about 1 cm. in diameter, shaped like a fruit stone, which also appears to be lying free. The mucosa in general is of normal color, but there are numerous small areas in the fundus and antrum, indicating erosions. The pylorus and antrum are well seen. Normal peristalsis is passing over the antrum. No polyp or carcinoma is visible, the only abnormality in the mucosa being the few erosions described. Diagnosis: foreign bodies of the stomach; superficial gastritis, with erosion.

Because of the underlying pyloric ulcer with pyloric obstruction these foreign bodies would not pass the pylorus, in spite of dietary regimen and belladonna. Although it would probably have been possible to remove these bodies through the open-tube gastroscope, it was thought that surgical intervention was indicated to treat the pyloric ulcer and that at the same time the foreign bodies could be removed. Laparotomy was therefore undertaken on May 11. An incision was made in the anterior wall of the stomach, and a prune stone and a plum stone were extracted. A definite ulcer was felt in the prepyloric region. The ulcer was resected, and a Finney pyloroplasty performed. The pathological report read "acute and chronic gastritis."

The convalescence was uneventful. Three and a half years after the operation the patient was seen in the Out Patient Department. She was symptom-free and had gained 20 pounds in weight.

Comment. This case represents an unusual type of gastrointestinal problem in which the final diagnosis was definitely established by gastroscopy.

DISCUSSION

From a study of the material presented above it is evident that gastroscopy has added greatly to

knowledge of disease of the stomach. Gastroscopy is a practical method of examination that gives us information regarding the color and detail of the gastric mucosa not obtainable in any other way.

Chronic gastritis is the commonest disease of the stomach; it is difficult to diagnose clinically, but easy by gastroscopy. Therefore patients with vague gastrointestinal complaints and negative x-ray examination should have gastroscopic examination. Hemorrhage from gastritis is now a well-recognized clinical entity. Severe bleeding may come from gastritis alone, and may occasionally call for gastric resection. Gastroscopic examination is necessary to establish a positive diagnosis and to follow the course of the disease. The examination should be made within a few days of the bleeding, since otherwise erosions and superficial ulcerations, which may have been the cause of severe hemorrhage, may have healed completely, leaving the diagnosis still in doubt. In cases of duodenal ulcer with hemorrhage the bleeding may in some cases be coming not from the ulcer but from the associated gastritis. The importance of recognizing this is obvious, for if surgery is to be undertaken a knowledge of the degree and extent of the gastritis is essential in order to plan an adequate operation. If there is very little gastritis a small partial resection may suffice; if there is moderate gastritis confined to the lower part of the stomach the resection should be planned accordingly; if there is very severe, extensive gastritis involving the upper part of the stomach, it may be advisable to continue medical treatment, postponing surgery indefinitely.

A diagnosis of gastric neurosis is not justifiable until gastroscopic examination has ruled out organic disease of the stomach. If chronic gastritis is present it may be the entire cause of the patient's symptoms or at least a major contributing factor. On the other hand, if no lesion is demonstrable either by x-ray or by gastroscopy the patient may rationally be treated for gastric neurosis. Similarly, when gastrointestinal symptoms persist in the presence of negative or inconclusive x-ray examinations, gastroscopy may establish a positive diagnosis. In fact, no gastrointestinal study is complete without gastroscopy.

Various problems arise in the diagnosis and treatment of peptic ulcer, some of which may be solved by direct inspection of the gastric mucosa. Gastroscopy may reveal one or more gastric ulcers not previously suspected. Such an observation will naturally modify the treatment. Direct inspection of an ulcer during treatment will be of assistance in evaluating the progress of the healing process. The demonstration of a severe gastritis in association with either a duodenal or a gastric ulcer will

sometimes modify the treatment and prognosis. A duodenal ulcer, for example, may appear to be healing, yet clinically the patient is getting worse; in some such cases it is the severe associated gastritis that is giving the symptoms. The question of cancer is always of great importance in gastric ulcer. By demonstrating that an ulcer has sharp margins and a clean base the gastroscopist can make a diagnosis of benign ulcer; if the margins are slightly irregular or the base dirty a diagnosis of cancer must be made. There are of course cases in which there will be doubt clinically, roentgenologically and gastroscopically; such cases must be regarded as cancerous until proved otherwise.

In suspected cancer of the stomach gastroscopy may establish a positive diagnosis. In occasional cases, when other methods of examination have failed, gastroscopy has demonstrated advanced carcinoma. Help may be given to the surgeon by the gastroscopic demonstration of the extent and operability of a gastric tumor. In the differential diagnosis of hypertrophic gastritis, carcinoma and lymphoma, gastroscopy, although not always giving the correct diagnosis, has been of definite assistance.

It is frequently said by roentgenologists that the stomach is difficult to examine postoperatively. In cases of postoperative gastritis, jejunal ulcer or recurrent neoplasm, gastroscopy has given valuable assistance. Postoperative gastritis is a distinct entity, which is impossible to evaluate or to treat satisfactorily without gastroscopy. Severe cases with hemorrhage may require further surgery.

In polyposis of the stomach, gastroscopy may differentiate true polyps from enlarged folds or foreign bodies, and in the former will demonstrate the broadness of the base and ulceration of the surface, vital factors in deciding the question as to whether malignant degeneration has occurred.

Let the reader receive the impression that gastroscopic examination is the final answer to all problems in gastric diagnosis, it should be pointed out that there are definite limitations to gastroscopy. There are a few patients who cannot be satisfactorily examined because of inability to extend the head, obstruction of the esophagus, spasm of the stomach, lack of co-operation and so forth. In ninety-nine cases out of a hundred, however, it is possible to effect a satisfactory introduction of the gastroscope. The examiner is then faced with the problem of visualizing all parts of the stomach. Because of the irregular shape of the organ certain areas are difficult to inspect, namely, the lesser curvature near the pylorus, the greater cur-

vature near the angulus and the posterior wall near the cardia. However, by proper manipulation of the instrument and the patient, and by observation during various phases of respiration and peristalsis, many of these so-called "blind areas" can be eliminated. A third difficulty is the correct interpretation of the findings. For example, the experienced observer knows that minor changes in the gastric mucosa may not be the cause of symptoms, that severe hypertrophic gastritis may be confused with an infiltrating type of carcinoma and that a benign gastric ulcer cannot always be differentiated from an early malignant gastric ulcer. Gastroscopy thus has its limitations. With increasing experience, however, and with improvements in the instrument, such as the biopsy forceps recently described by Kennamore,¹² gastroscopic examination is bound to play an increasingly important role in the diagnosis and treatment of gastric disease.

CONCLUSIONS

Gastroscopy is now a generally accepted method of examining the stomach. It bears much the same relation to gastroenterology that diagnostic cystoscopy bears to urology.

Gastroscopic examination is easily conducted in the outpatient department with the aid of only one assistant. The technic of local anesthesia is simplified by merely having the patient gargle with a 2 per cent solution of Pontocaine. A specially trained head-holder is unnecessary, since the procedure is very satisfactorily carried out with the head resting on small pillows.

The various indications for gastroscopy are given and 12 illustrative cases are presented and discussed.

REFERENCES

- Schindler, R.: *Gastroscopy: the endoscopic study of gastric pathology*. 343 pp. Chicago: University of Chicago Press, 1937.
- Benedict, E. B.: Examination of the stomach by means of a flexible gastroscope: a preliminary report. *New Eng. J. Med.* 210:669-674, 1934.
- Jones, C. M., Benedict, E. B., and Himpton, A. O.: Variations in the gastric mucosa in pernicious anemia: gastroscopic, surgical and roentgenologic observations. *Am. J. M. Sc.* 190:596-610, 1935.
- Benedict, E. B.: Hemorrhage from gastritis: a gastroscopic study. *Am. J. Digest. Dis. & Nutrition* 4:657-664, 1937.
- Ruddock, J. C.: Peritonoscopy. *Surg., Gynec. & Obst.* 61:623-630, 1937.
- Benedict, E. B.: Peritonoscopy. *New Eng. J. Med.* 218:713-719, 1938.
- Schitzki, R.: The comparative value of gastroscopy and roentgen examination of the stomach. *Radiology* 29:488-491, 1937.
- Ansprenger, A., and Kirklind, B. R.: Roentgenologic aspects of chronic gastritis: critical analysis. *Am. J. Roentgenol.* 38:533-541, 1937.
- Benedict, E. B.: Gastroscopic observations in neoplasm. *New Eng. J. Med.* 214:563-566, 1936.
- Benedict, E. B., and Allen, A. W.: Adenomatous polypi of the stomach: with special reference to malignant degeneration. *Surg., Gynec. & Obst.* 58:79-84, 1934.
- Upton, C., and Jackson, C. L.: *Bronchoscopy, Esophagoscopy and Gastroscopy: A manual of peroral endoscopy and laryngeal surgery*. Third edition. 485 pp. Philadelphia: W. B. Saunders Co., 1934.
- Kennamore, B.: personal communication.

PULMONARY INFARCTION AS A CAUSE OF PNEUMOTHORAX

JOSEPH H. MARKS, M.D.*

BOSTON

SPONTANEOUS pneumothorax is an infrequent complication of pulmonary disease as seen in a general hospital. There is frequently, and quite properly, a tendency to attribute the condition to tuberculosis, but if there is little or no evidence of a pre-existing tuberculous infection, other causes should also be considered. The standard textbooks of medicine list a variety of conditions as possible causes of spontaneous pneumothorax and are in general agreement as to their relative importance as etiologic factors. During recent years, attention has been called to the frequency of rupture of an emphysematous bleb as the reason for an otherwise unexplained pneumothorax. It is agreed that an infarct, if septic, may break down and permit the passage of free air into the pleural cavity. It is fortunate that the latter does not often happen, since pulmonary infarction is a not uncommon complication in postoperative patients and in others whose circulation is inadequate.

Infarcts of the lung are usually of recent origin when first seen, and they will usually be found to have changed appreciably in size or radiographic density if repeated examinations are made during the ensuing few days. This relatively rapid change in the lesion as shown on serial roentgenograms calls attention to the fact that the process is an acute one and therefore unlike the usual tuberculous process, which, though active, is not likely to change definitely in appearance within the space of a few days. If necrosis occurs within the infarcted area and pneumothorax results, there is likely to be a rapid outpouring of purulent exudate, thus giving rise to a pyopneumothorax.

Pulmonary infarction is secondary to a pathologic process elsewhere in the body. If, therefore, a pneumothorax is found in a patient known to have a disease that may give rise to the formation of emboli, infarction should be considered as a possible cause of the pneumothorax. The possibility becomes a probability if an area of consolidation is present at or near the base of the lung, and especially if there is an inflammatory process elsewhere in the body. The following two cases are illustrative of these facts.

CASE REPORTS

CASE 1 (N. E. D. H. 86423). The patient was a 17-year-old boy who was first seen in the New England Deaconess Hospital in March, 1937, at which time he was suffering

*Roentgenologist, New England Deaconess Hospital.

from a moderately severe ulcerative colitis of recent onset. He was under the care of Dr. E. P. Joslin and his associates. He remained in the hospital 36 days and during the latter part of his stay had only one stool daily. During this time he gained 8 pounds, and the temperature and pulse were essentially normal.

The patient was readmitted to the hospital during August, 1937, and again in June, 1938, because of recurrence of the diarrhea, with the occasional passing of blood.

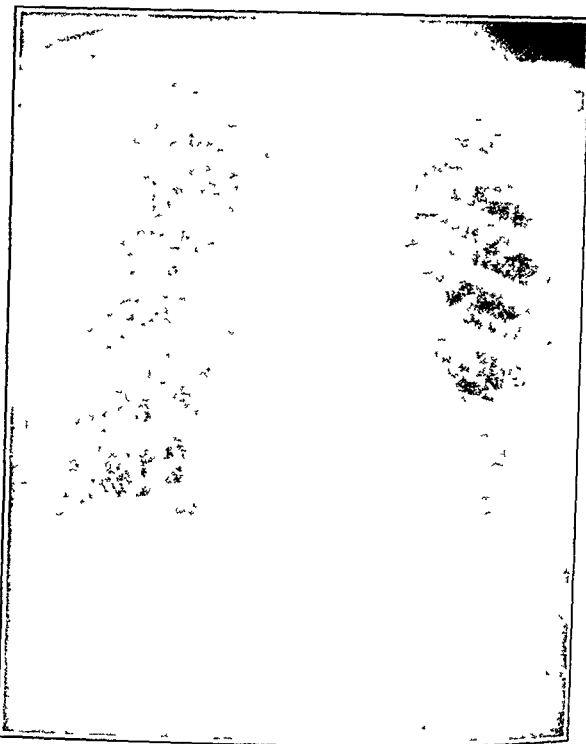


FIGURE 1. Case 1.

This film was taken on the third hospital day. There is consolidation at the left base laterally.

Proctoscopy and roentgen examination with barium enema showed findings characteristic of ulcerative colitis. He was discharged on July 12, 1938, and it is interesting that the record shows that physical examination of the chest on that day was entirely negative.

The patient was again admitted to the hospital 10 days later, this time because of nausea, vomiting and hematemeses. There had been no cough or dyspnea. He stated that he had vomited some dark, bloody material, and was sure that this had not been coughed up. Physical examination showed a pale, slightly cyanotic young adult who was perspiring freely. The temperature was 102°F., and the pulse 120. The lungs were clear except for a triangular area in the left axilla, over which there was some dullness, and diminution of breath sounds. X-ray examination of the chest with a bedside unit on the 3rd hospital day showed an area of consolidation at the left base laterally, including the costophrenic angle and extending upward to the level of the 4th rib in the axilla. A second exam-

ination on the 19th hospital day showed a slight decrease in size and density of the area of consolidation previously noted, but there was then a small amount of free air in the left pleural cavity, and a new area of partial consolidation opposite the right second interspace.

One week later the degree of pneumothorax on the left was somewhat more marked, the degree of collapse of the lung being estimated at 60 per cent. Several areas

found in several branches of the pulmonary artery on the right, but none were found on the left. Injection of air into the left main bronchus failed to demonstrate the point of leakage. The descending colon showed several irregular, superficial areas of ulceration, with hyperemia of the surrounding mucosa. In the right internal and external iliac veins there was a closely adherent thrombus that varied from red to gray. All other organs and tissues were essentially normal.

CASE 2 (N E D H 97823) A 24 year-old, unmarried, man was admitted to the hospital on July 29, 1939, on the medical service of the Lahey Clinic, with a complaint of increasing weakness and shortness of breath. He had been well until 1 year previously, when he had developed a hacking, nonproductive cough. He had consulted a local physician and been told that he had heart trouble. He had given up his work as a counterman and had been fairly well until 3 months before admission, when he had consulted another physician and had been told he had thyroid trouble. During the 10 weeks prior to admission he had been a patient in a nearby hospital. He had lost a total of 80 pounds during the year.

He had had scarlet fever and probably also tonsillitis but there was no history of rheumatic fever, pleurisy, pneumonia, influenza, tuberculosis, gonorrhea or syphilis. Physical examination showed a pale, slightly jaundiced young male adult who was dyspneic and orthopneic. The



FIGURE 2 Case 1

This film was taken on the twenty sixth hospital day. There is pneumothorax, with partial clearing of the consolidated area.

of diminished density within the original area of consolidation suggested multilocular cavity formation.

There was some cough and expectoration at this time, and examination of the sputum showed a few suggestive acid fast organisms. Subsequent examinations failed to show similar organisms, and a guinea pig inoculated with the sputum revealed no evidence of tuberculosis.

On the 22nd hospital day it was noted that the general condition was distinctly worse. There was elevation of the pulse and respiratory rates, and slight cyanosis. On the following day the patient complained of pain in the right thigh, but there was no redness or swelling. The temperature at this time was 103°F, but it subsequently fell gradually, and was practically normal at the time of his death on the 38th hospital day. The pulse rate remained elevated. During this stay in the hospital he had passed two or three loose stools daily that showed positive benzidine tests for blood on almost all examinations, although there had been no gross bleeding.

Autopsy There was free air in the left pleural cavity, and adhesions extending from the region of the interlobar fissure to the parietal pleura in the axillary line. The right and left lungs weighed 600 and 410 gm, respectively. Several areas of consolidation were present in each lung. These were roughly pyramidal in shape, with their bases at the pleural surface. Adherent thrombi were

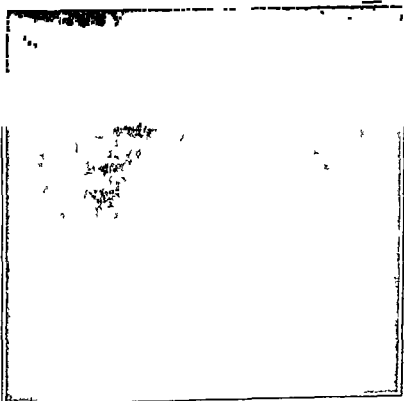


FIGURE 3 Case 2

Hydropneumothorax, with an Area of Consolidation on the Opposite Side

extremities were cold and slightly edematous. There was dullness at the left base with diminished breath sounds, and there were rales at both bases. The heart was greatly enlarged and showed a gallop rhythm and a systolic murmur at the apex. The liver edge extended about 5 cm below the costal margin. There was no clubbing of the fingers, and no petechiae were seen. The blood pressure was 110/70. The red-cell count was 3,600,000, and the white cell count 18,750. The serum protein was 4.9 gm per 100 cc, and the nonprotein nitrogen 86 mg per 100 cc. An electrocardiogram taken on the day of admission showed slurring of the QRS complex in all leads, left axis deviation and slight inversion of T₁.

Respiration was improved following withdrawal of about 2500 cc. of amber-colored fluid from the left pleural cavity. Digitalization and the intravenous administration of Salyrgan produced a moderate diuresis, with decrease in size of the liver and disappearance of the edema of the lower extremities. The nonprotein nitrogen in the blood gradually increased in amount, and the breath became urinous.

On the 18th day the patient developed pain in the right lower thorax, accompanied by an increase in the pulse and respiratory rates. X-ray examination of the chest at this time showed a hydropneumothorax on the right, with approximately 80 per cent collapse of that lung, and with a slight shift of the mediastinum toward the left. There was an area of mottled consolidation in the left lung opposite the 2nd interspace anteriorly. The heart appeared moderately enlarged. X-ray examination on the 2nd day had shown high position of both diaphragms, congested lungs, a small amount of fluid in the right pleural cavity and enlargement of the heart, but no evidence of pneumothorax.

There was a rapid increase in dyspnea, and since the findings suggested a positive pressure pneumothorax, a needle was inserted in the right pleural cavity. The initial pressure was equivalent to 9 cm. of water, but after removal of 1700 cc. of air, the pressure was 2 cm. on expiration, with a negative pressure of 5 cm. on inspiration. The withdrawn air had a foul odor suggesting hydrogen sulfide. Death occurred 2 days later.

Autopsy. The right pleural cavity was opened under

water. Foul gas escaped under pressure, and there was also 3000 cc. of greenish-brown fluid having a foul odor. The pleura was thickened and was covered by a shaggy exudate. The left pleural cavity was not remarkable. The pericardial cavity contained 400 cc. of clear, brownish fluid, and the pericardium was covered with a shaggy exudate. The heart weighed 620 gm., but its valves and coronary arteries were normal. The cut surface of the myocardium was a deep red, with scattered streaks of brownish yellow near the apex. The right and left lung weighed 440 and 320 gm., respectively. The right upper lobe and both lobes on the left contained several firm foci measuring 2 to 3 cm. in diameter. The right middle and lower lobes were gangrenous. An adherent, gray thrombus was found in one of the branches of the right pulmonary artery. Other findings included an adrenocortical adenoma and a mid-zonal cirrhosis of the liver.

SUMMARY

Two proved cases of pneumothorax resulting from pulmonary infarction are presented. Although pneumothorax is a rare complication of infarction, it is believed that the clinical history and roentgen findings are sufficiently clear in most cases to suggest the correct diagnosis.

I am indebted to Drs. E. P. Joslin and F. H. Lahey for their permission to report these cases.

195 Pilgrim Road

THE SIGNIFICANCE OF CHARCOT-LEYDEN CRYSTALS*

JAMES H. THOMPSON, M.D.,† AND FRANKLIN K. PADDOCK, M.D.‡

BOSTON

THE crystals now known as Charcot-Leyden crystals were first described in 1853 by Charcot and Robin,¹ who found them in the heart's blood and the spleen of a patient who died of leukemia. It was not until twenty years later that they were described by Leyden,² who found them in "asthmatic" sputum and who, because of slight variations in solubility, considered them different from those originally described by Charcot. Even before this second description, Böttcher³ had found in prostatic secretion crystals that for the next three decades were generally accepted as identical with the Charcot crystals. As a result, considerable confusion arose in the literature; in fact, much of the chemical investigation done on the crystals obtained from prostatic secretion was incorrectly applied to the Charcot-Leyden crystals.^{4, 5} The latter were first described in this country in a case of leukemia by White⁶ in 1859. In 1895, Cohn⁷ reviewed the literature and concluded that the crystals found in leukemic blood, in asthmatic sputum, in nasal polyps and in bone marrow differed from those

found in prostatic secretion. The relation of Charcot-Leyden crystals to eosinophils was first emphasized by Schwarz⁸ in 1914. In 1921, Liebreich's⁹ description of the appearance of the crystals in normal blood reawakened interest in the subject. This description was confirmed by Neumann¹⁰ several years later. Wrede,¹¹ in 1927, revived the older theory of the relation of the prostatic to the leukemic crystals, and by questionable chemical methods showed a higher concentration of "spermin" in leukemic than in nonleukemic spleens. Since then the literature^{12, 13} has been chiefly confined to an occasional observation of Charcot-Leyden crystals in various pathologic conditions such as eosinophilia of unknown cause and periarteritis nodosa. Turner et al.¹⁴ in 1936, suggested that the substance in the eosinophil apparently responsible for the so-called "Gordon phenomenon" was the Charcot-Leyden crystal, although the reference they gave contained no mention of such a relation.

The present study deals with attempts to demonstrate Charcot-Leyden crystals in blood and tissues and to determine their nature.

*From the Medical Clinic, Peter Bent Brigham Hospital.

†Formerly fourth-year student, Harvard Medical School.

‡Formerly assistant resident in medicine, Peter Bent Brigham Hospital.

METHODS

In the routine demonstration of Charcot-Leyden crystals a drop of the material to be examined was placed on a glass slide and protected from evaporation by shielding it with a coverslip ringed with vaseline. The slide thus prepared was allowed to stand at room temperature for at least a week and was examined daily under the microscope. The Charcot-Leyden crystal was considered to consist of two symmetrical, six-sided pyramids joined base to base. They were always readily identifiable un-

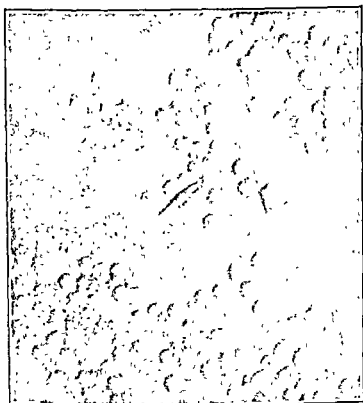


FIGURE 1. Photograph of a Charcot-Leyden Crystal in the Blood of a Patient with Periarthritis Nodosa.

der the high dry lens of the microscope, varying in length from one half to three times the diameter of an erythrocyte (Figs. 1 and 2). Usually they were first seen on the fourth day.

SOURCES

From 100 routine hospital medical admissions, drops of finger blood were obtained and a wet smear was made. The patients represented a variety of diseases including hypertension, chronic nephritis, heart disease, pernicious and aplastic anemia, peptic ulcer, pneumonia, carcinoma and various types of lymphoma, including myelogenous and lymphatic leukemia, lymphosarcoma and Hodgkin's disease. The white-cell counts ranged from 3000 to 240,000, and the percentages of eosinophils from 0 to 25, the highest figure being associated with a leukopenia. The blood of none of these showed an absolute increase of the eosinophils, and in no blood were Charcot-Leyden crystals demonstrated.

Several patients were studied in particular because of their disease or because of an unusual

eosinophilia. Of 5 patients with bronchial asthma with an average eosinophilia of 8 per cent, none showed crystals in the blood. One patient with chronic ulcerative colitis had typical crystals in the stools but not in the blood. Of 3 patients with chronic myelogenous leukemia, 2 showed a number of crystals in the blood. Their respective white-cell counts were 55,000, with 12 per cent eosinophils, and 78,000, with 14 per cent eosinophils. Two cases of presumed periarthritis nodosa showed Charcot-Leyden crystals in large numbers in the blood by the usual wet-smear method; the white-cell counts were 20,000, with 70 per cent eosinophils, and 40,000 with the same percentage of eosinophils. One case of presumed trichiniasis with a white-cell count of 16,000 and a 20 per cent eosinophilia showed an equally large number of crystals.

The blood of horses used for the production of

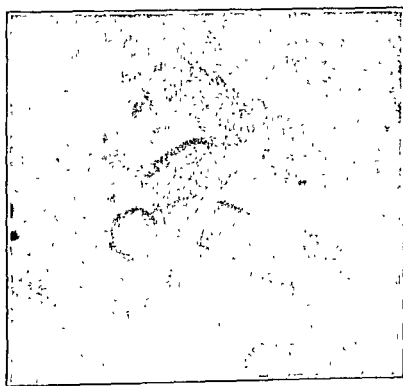


FIGURE 2. Photograph of Four Charcot-Leyden Crystals in a Bronchiolar Mucous Plug in a Patient Dying of Bronchial Asthma (highly magnified).

The crystal on the left is cut across and shows the hexagonal shape.

anti-serum,* studied by the usual method, showed little eosinophilia and no crystals.

Normal rabbits' blood showed no crystals even though their neutrophilic cells have an eosinophilic cast.

Five guinea pigs were inoculated with *Trichinella spiralis*. The maximum eosinophilia thus obtained was 20 per cent, with a white-cell count of 10,000. No crystals were obtained.

Prostatic secretion, obtained post mortem, produced no Charcot-Leyden crystals on standing for a week. After the addition of lead acetate to a

*Obtained through the courtesy of the Antisera and Vaccine Laboratory, Massachusetts Department of Public Health.

filtered alcoholic solution of the secretion as described in the literature,¹⁵ quadrilateral crystals were found, which because of the number of plane surfaces, lack of symmetry, and spindling tendency we did not consider characteristic of Charcot-Leyden crystals. They did, however, resemble those crystals depicted in the literature as being typical of "spermin."¹⁶

The work of Liebreich⁹ was repeated in part in an attempt to produce Charcot-Leyden crystals from normal blood. The various methods that he proposed consist essentially of a concentration of the white-cell layer. Contrary to his claim, eosinophils were not thus produced, nor were Charcot-Leyden crystals found after allowing a wet smear of such a preparation to stand. After several days, long spindling crystals, without plane surfaces, appeared and were thought possibly to be fibrin.

Microscopical sections of tissues from 11 fatal cases of myelogenous and lymphatic leukemia were examined. The preparations from only 1 case showed the crystals; they were visible in all tissues of the body and were most plentiful in the pancreas and spleen. This patient had myelogenous leukemia. Only occasional eosinophils were found in the peripheral blood, but eosinophils were markedly increased in the bone marrow and lymph nodes. Of 7 patients with ulcerative colitis in whom sections of the colon were examined post mortem, 1 showed a marked increase of eosinophils in the submucosa, with occasional small Charcot-Leyden crystals.

Slides of the lungs obtained from 8 fatal cases of bronchial asthma were reviewed. In 1 case crystals were found in the mucus plugging the smaller bronchioles.

NATURE OF THE CRYSTALS

The exact nature of Charcot-Leyden crystals has never been determined. Earlier investigations have been clouded by confusion with the crystals obtained from prostatic secretion. In the earlier literature it is said^{7, 15} that Charcot-Leyden crystals are soluble in hot water, acetic acid, tartaric acid, phosphoric acid, potash and sodium, but not in cold water, alcohol, ether, chloroform and glycerin.

Using the blood obtained from a case of trichiniasis, where Charcot-Leyden crystals of a typical shape had been found in great numbers, the solubility of the crystals was tested in tap water, distilled water, ethyl alcohol, glycerin, sodium hydroxide, formalin, acetic acid, sulfuric acid and nitric acid, all in various dilutions. In all these solutions the crystals were dissolved or destroyed, disappearing by fragmentation at varying speeds.

Neither by drying nor by adding substances of the opposite reaction, nor by further dilution, were the crystals again seen in solutions so treated.

A small hanging-drop preparation of the crystals was incubated with pepsin for forty-eight hours. At the end of this time the crystals had disappeared. In a similar preparation incubated without pepsin but with physiological saline solution the crystals persisted, apparently unchanged.

Because of the work of Code and MacDonald¹⁷ suggesting some parallelism between human eosinophils and a histamine-like substance, both normal and eosinophilic blood samples were combined in various dilutions with histamine and histaminase. Wet-smear preparations of these mixtures produced no Charcot-Leyden crystals.

DISCUSSION

It is apparent from this study that the appearance of Charcot-Leyden crystals, when considered only in their typical form, shows a close relation to eosinophils, since the crystals were found in blood where a high absolute eosinophilia existed, whereas they were not demonstrable by the same technic when eosinophils were not present in abnormally high numbers. This association has been pointed out in the literature and in general has been found to be true wherever the crystals have appeared.⁸

According to our work and according to the literature, the crystals are apparently not specific for any disease. They have been found in the blood from cases of the lymphoma group, periarthritis nodosa, trichiniasis and other diseases associated with an eosinophilia^{12, 13}; in the stools of patients with a variety of intestinal infections¹⁶; in the sputum of asthmatic patients and those with other types of bronchial disease^{3, 12}; in pleural fluids¹⁹; and in such localized collections of eosinophils as nasal polyps and skin blebs.⁸ In all these cases the relation of the crystals to the eosinophils seems to hold true.

The nature of the crystals is not known. No recent chemical work has been done on the subject, and the crystals have never been isolated from the materials in which they were found. The chemical determinations done on prostatic secretion do not apply, since the true Charcot-Leyden crystal shows a different architectural pattern and has never been proved to be identical or transmutable chemically. The isolation and analysis of these crystals should help in the understanding of the eosinophil.

SUMMARY

Typical Charcot-Leyden crystals were found in the blood of all patients with a high absolute

eosinophilia, but were not found in the 102 cases where eosinophilia was not present. They were also found in suitable preparations of tissues with a marked local eosinophilia.

Investigation of the blood of guinea pigs, horses and rabbits, after the administration of various stimuli, yielded no crystals; however, the blood eosinophilia never reached a high absolute level.

Attempts to isolate the crystals from the blood were unsuccessful. In a variety of solutions tried they were either dissolved or destroyed.

The crystals do not appear to be typical of any specific disease, but seem rather to be associated with eosinophilia, whether generalized or localized.

REFERENCES

- Charcot, J. M., and Robin, C. Observation de leucocythémie. *Mém de Soc de Biol* 5 44 50 1853
- Leiden, E. Zur Kenntnis des Bronchial Asthma. *Virchows Arch f path Anat* 54 324 352, 1872.
- Böttcher, A. Farblose Krystalle eines eiweissartigen Körpers aus dem menschlichen Sperma dargestellt. *Virchows Arch f path Anat* 32 523 535, 1865
- Schreiner, P. Ueber eine neue organische Basis in thierischen Organismen. *Ann d Chem* 194 68 84, 1878
- Majert, W., and Schmidt, A. Ueber das Piperazine (Hoffmann's Diäthylendiamin, Ländenburg's Aethylenamin, Schreiner's Spermin). *Ber d deutsch Chem Gesellsch* 23 3718 3726 1890
- White, J. C. Leukosis. *Boston M & S J* 60 89 94, 1859
- Cohn, T. Beitrag zur Kenntnis des Charcot'schen und Böttcher'schen Krystalle. *Deutsches Arch f klin Med* 54 515-524, 1895
- Schwarz, E. Die Leukose von der allgemeinen und örtlichen "Eosinophilie". *Ergebn d allg Path u path Anat* 17:137 789, 1914.
- Liebreich E. Le sang in vitro éosinophile, fibrinogénèse, phagocytose et hématies. 128 pp. Paris. Masson et Cie. 1921
- Neumann A. Ueber die Natur der Charcot Leyden Böttcher Neumann Krystalle. *Zischr f physiol Chem* 173 69 71, 1927
- Wrede, F. Boldt, F., and Buch, E. Ueber die Natur der Charcot Leyden Böttcher Neumann Krystalle. *Zischr f physiol Chem* 165, 155 166, 1927
- Bahrman E. Ueber ein gleichzeitiges Vorkommen von Asthma bronchiale mit rheumatischer eosinophiler Gefässentzündung. *Virchows Arch f path Anat* 296 277 288 1935
- Thomson, A. P., Wilson, G. H., and McDonald S. Three cases of unusual illness with eosinophilia one with lesions in the liver resembling those of tularemia. *Lancet* 2 9 13, 1937
- Turner, J. C., Jackson, H. J., and Parker, F. Jr. The etiologic relation of the eosinophil to the Gordon phenomenon in Hodgkin's disease. *Am J M Sc* 195 27 32, 1938
- Oppenheimer C. *Handbuch der Biochemie* Vol I 932 pp. Jena Gustav Fischer, 1909 Pp 816 818
- Poehl, A. Der Nachweis des Spermins in verschiedenen Drüsen des thierischen Organismus und die chemische Zusammensetzung des Brown-Séquard'schen Heilmittels. *Deutsche med Wchnschr* 18 1125 1128 1892
- Code, C. F., and MacDonald A. D. The histamine like activity of blood. *Lancet* 2 730 733 1937
- Acron H. W. The significance of Charcot Leyden crystals in the faeces as an indication of amoebic colitis. *Indian J M Research* 6 157 161, 1918
- Floderer, H. Ueber Charcot Leyden'sche Krystalle im Ejacemester. *Wien Klin Wchnschr* 16 276 279, 1903

REPORT ON MEDICAL PROGRESS

ARTERIAL HYPERTENSION*

SOMA WEISS, M.D.†

BOSTON

THE pathogenesis of arterial hypertension, so far as the underlying physiologic and morphologic processes are concerned, is fairly well established. The relation of certain types of arterial hypertension to renal ischemia has been demonstrated conclusively through experimentation. There is evidence for the presumption that humoral agents of renal origin cause hypertension. However, the biologic nature of the mechanism operating between renal ischemia and hypertension, although the subject of intense investigation, remains to a large extent obscure, particularly in man. Furthermore, there is still much to be learned in the treatment of hypertensive cases.

HYPERTENSION IN MAN

Although many investigators have emphasized the fact that arterial hypertension is but a symptom of derangement of the arteriolar system, physicians are basing too-rigid judgments of the state of the arterial system and the prognosis of the pa-

tient on single measurements of the arterial pressure taken under different conditions. Robinson and Brucer¹ have analyzed the variations in normal blood pressure in a statistical and clinical study of 11,383 persons. The normal range of pressure is considered as 90 to 120 systolic, and 60 to 80 diastolic. About two thirds of the group had pressures below 125 systolic and 80 diastolic. These investigations demonstrate once more the fact that arterial hypertension should not be considered a disease, and that slight or moderate elevation above the normal range should be interpreted with caution. Ayman and Goldshine² rightly point out that the present knowledge of essential hypertension is based on measurements of blood pressure made by physicians, largely in the clinic or office. Hardly any data are available regarding the level of blood pressure obtained during a patient's normal routine of living. For this reason these physicians studied 34 patients with various degrees of essential hypertension, whose blood pressures were recorded over a long period in the clinic and at home. The home readings were taken twice daily for weeks or months by the patient or a member of the household. This study reveals that the home

From the Medical Clinic of the Peter Bent Brigham Hospital and the Harvard Medical School.
†Professor of the theory and practice of physic, Harvard University; physician-in-chief, Peter Bent Brigham Hospital.

systolic and diastolic blood-pressure readings are lower than the clinic readings in all cases of essential hypertension. In 30 per cent of the cases the systolic home blood-pressure readings were 40 or more lower than those in the clinic, and in 24 per cent the diastolic home readings were 20 or more lower. The method of frequent blood-pressure readings caused no neurosis or harm in any patient. Those patients with only slight differences between home and clinic readings had in general comparatively little fluctuation of blood pressure from day to day.

The investigation of the physiologic mechanisms underlying arterial hypertension has been carried farther by Stead and Kunkel,³ who conclude that the increased peripheral resistance offered by the arteriolar system is distributed in a fairly uniform way throughout the body, including the brain. It is of interest that increased vascular resistance was found also in the minute arterial vessels of the voluntary muscles. In the regulation of the tone of these vessels, nervous influences play little or no role as compared with chemical agents. The inference is that in the vasoconstrictor state of the arterioles of the voluntary muscles, humoral factors must be active.

Hines⁴ reports again on his experience with the response of the arterial pressure to the cold-pressor test. He outlines the sources of variation in the responses of subjects with arterial hypertension, and claims that under adequately controlled conditions, the response in the same patient is on the whole uniform. Elevation is relatively more significant in the diastolic than in the systolic pressure. Hines considers that a rise of more than 20 systolic and more than 15 diastolic is indicative of a hypertensive, vasoconstrictor mechanism. In persons with arterial hypertension or "tendency" to hypertension the response to the cold-pressor test is increased as much as two to four times that in normal persons. An increased response was noted also in a group of persons with normal pressure who had had hypertension previously or who showed hypertensive eyeground changes. (It is probable that this increased response, like the increased vasoconstrictor response to psychic, painful or other noxious stimuli, is an expression of increased vasoconstrictor irritability of the vessels.) The results obtained by Miller and Bruger⁵ indicate that the cold-pressor test is less reliable as a diagnostic aid. These investigators found that 39 per cent of the normal group and 76 per cent of the group with essential hypertension gave a hyperreactor response. It is interesting that in elderly persons with essential hypertension and evidence of nephrosclerosis, the response to the pressor

test was less marked than in younger persons with essential hypertension. Patients with chronic nephritis often had a normal reaction. Thomas and Warthin⁶ undertook the study of a cold-pressor test under controlled conditions in normal dogs and in those with renal hypertension. In 90 per cent of the tests on the normal group and in 87 per cent on the animals with hypertension, no pressor reaction of over 22 was observed. (On the basis of the available literature and on the basis of personal experience with this test and with other vasoconstrictor reactions in persons with normal and with elevated arterial pressure, I consider that at best the cold-pressor test has somewhat limited significance and applicability.)

Weiss, Dexter, Parker and Tenney⁷ report on a systematic study of the nature of arterial hypertension in pregnancy, with particular reference to the toxemic syndrome of pregnancy (pre-eclampsia and eclampsia). There is considerable confusion about the definition, physiologic and structural changes, pathogenesis and etiology of these conditions. These investigators conclude that evidence of some degree of generalized edema was present in 64 per cent of all normal pregnant women who were studied as controls. The physical and chemical characteristics, the distribution, and the time of onset and of post-partum disappearance of the edema of normal pregnancy are similar to or identical with those of the edema associated with toxemia (pre-eclampsia and eclampsia). At times the generalized edema of normal pregnancy, like that of toxemia, can persist for weeks or months after delivery. In 7 per cent of the normal pregnant women with generalized edema, symptoms such as frontal headaches, visual disturbances, nausea and vomiting—similar to the symptoms seen in toxemia or in severe premenstrual edema—were noted, and in these patients a close relation was found between the cerebral symptoms and the daily appearance, usually in the morning, and disappearance of facial edema. In one patient with severe generalized edema, but with normal blood pressure and no proteinuria, eclamptiform convulsions occurred. The mechanism of the edema of normal pregnancy, like that of pre-eclampsia and eclampsia, could not be explained by any of the usual causes for edema formation. By exclusion, a chemical or hormonal etiology resulting in retention of water and electrolytes in the tissues is suspected.

The same authors emphasize that not all types of hypertension observed in pregnancy should be considered as "toxemia." Prepregnant hypertension uninfluenced by pregnancy and hypertension developing or accentuated during pregnancy should

be differentiated. Only the latter is a phase of toxemia. About half the patients with hypertension of varied etiology before their pregnancy had no aggravation of the hypertensive state during pregnancy, and had no evidence of toxemia. The two most important factors predisposing to pre-eclampsia and eclampsia are pre-pregnant hypertension and generalized edema. Pyelonephritis and other nephritides predispose to toxemia only so far as they are associated with hypertension and edema. The significance of symptoms and signs of pre-eclampsia and eclampsia is discussed in this report.

From a study of the etiology of toxemia, they conclude that death of the fetus in utero usually does not result in improvement. Following fetal death, hormones originating in the placenta usually continue to be eliminated in the urine, indicating continued activity of the placenta. These workers claim that there is no valid evidence that pressure on the ureter or renal artery is responsible for pre-eclampsia or eclampsia. The conclusion is reached that the presence of a *functioning* placenta maintains the syndrome, and that removal of the placenta is responsible for improvement.

They also state that sustained hypertension follows toxemia in about one third of the patients with normal blood pressure before pregnancy. In these cases toxemia induces permanent "post-toxemic" hypertension. In general the longer the existence of the toxemia, the greater is the tendency to sustained post-partum hypertension. The characteristic morphologic changes of toxemia present in the placenta, kidneys and liver are described. The renal changes consist of a type of glomerulonephrosis. Structural changes in the minute vessels of the kidney can develop within a few weeks in the presence of toxemia. It is concluded that, among the underlying causative factors, chemical substances originating in the placenta are primarily responsible for the syndromes.

Schroeder and Steele⁸ have attempted to classify essential hypertension on the basis of the relation of presenting phenomena to renal, nervous, endocrine and vascular symptoms. It is questionable whether this classification is rational or serves a constructive purpose. Williams and Harrison⁹ proposed a classification based partly on underlying causative factors and partly on aggravating factors. In this classification, Group I includes hypertension of neurogenic origin; Group II includes cases of endocrine origin; Group III includes cases with renal diseases, such as acute and chronic nephritis, urinary obstructions and renal arterial disease; Group IV includes hypertension of metabolic origin such as hypercholesterolemia and gout

associated with renal vascular lesions; Group V includes cases of hypertension caused by congestive failure of the heart; and Group VI includes unclassified cases. Weiss,¹⁰ discussing the clinical and physiologic characteristics of arterial hypertension, proposes the following classification of types of clinical hypertension:

- I. Hypertension of organic vascular origin, with renal ischemia.
 1. Congenital malformations.
 - a. Coarctation of the aorta.
 - b. Hypoplastic renal artery.
 - c. Polycystic kidneys.
 2. Inflammatory vascular diseases.
 - a. Glomerulonephritis.
 - b. Pyelonephritis.
 - c. Periarthritis nodosa.
 - d. "Rheumatic" arteritis.
 - e. Disseminated lupus erythematosus.
 3. Degenerative vascular diseases.
 - a. Arteriosclerotic occlusive lesions of the renal artery (essential hypertension).
 - b. Renal arteriosclerosis.
- II. Hypertension of organic vascular origin, without renal ischemia (diffuse arterial and arteriolar sclerosis).
- III. Hypertension of nonorganic vascular origin.
 1. Endocrine disorders.
 - a. Pituitary dysfunction and neoplasms (Cushing syndrome).
 - b. Adrenal dysfunction and neoplasms (cortical and medullary).
 - c. Certain types of toxemia of pregnancy.
 2. Nervous disorders.
 - a. Cerebral trauma.
 - b. Cerebral neoplasms.
 - c. Poliomyelitis.
 - d. Rare vascular diseases of the brain.

This classification does not include the secondary factors that accentuate hypertension—that is, emotions, complete heart block, aortic insufficiency and so forth. Carotid-sinus reflexes, bichloride of mercury, lead, tobacco, alcohol, syphilis, hydro-nephrosis, prostatic obstruction, spinal bladder and infarcts of the kidney are not considered *primary* causative factors of hypertension. So-called "malignant" hypertension is held to be only a special type of severe spastic and structural vascular response, which can develop in any type of hypertension. Although renal ischemia is considered today the most important cause of hypertension, diffuse arterial and arteriolar sclerosis (Group II), irrespective of renal involvement, is still included in this etiologic classification of hypertension. At present it is not known whether in essential hypertension with renal arteriosclerosis the local degenerative process is a primary process, or whether the

arteriosclerosis is preceded by a renal vasospastic stage caused by humoral agents of renal or extra-renal origin.

Rosenberg¹¹ has studied the symptoms and the histologic changes in the brains of 17 patients with the malignant type of hypertension. He found the cerebral symptoms in these patients frequently associated with such organic lesions as increased intracranial pressure resulting from cerebral edema, multiple microscopic cerebral lesions and vascular accidents involving the larger vessels.

Stead and Kunkel¹² have investigated the nature of the transient hypertension induced in man by Paredrinol. It is pertinent to note that, in contrast to the hypertension induced by adrenalin or other sympathomimetic drugs, this hypertension is characterized by several factors that are similar to or identical with those observed in spontaneous human hypertension. The cardiac output, circulation time and basal metabolism remain normal. The decrease in the heart rate depends on stimulation of the carotid-sinus reflex. De Wesselow and Thomson¹³ have investigated the effect of certain electrolytes particularly sodium and potassium, on the level of the arterial pressure. Variations in the dietary intake of these substances have little or no effect on the level of the arterial pressure. With the administration of unusually large amounts of sodium, the blood pressure rose, whereas an excessive amount of potassium had the opposite effect. The rise apparently depended on increase in blood volume caused by the sodium, and the fall on the effect of potassium on the heart.

EXPERIMENTAL HYPERTENSION OF RENAL ORIGIN

Experimental investigation of the nature of the interrelation between the kidney and the arterial pressure has continued vigorously. Page¹⁴ has reported one more method of inducing arterial hypertension of renal origin, namely, the use of a cellophane envelope to produce collagenous perinephritis, which in turn causes renal ischemia and hypertension. This hypertension, which is similar to that induced by other forms of renal ischemia, persists after renal denervation but is abolished by bilateral adrenalectomy. Greenwood, Nassim and Taylor¹⁵ considered the possibility that the release of the renal pressor substance was a physiologic response to a disproportion between the work required of the kidney and its available blood supply. If this concept were true, it followed that it should be possible to produce hypertension by preventing the hypertrophy of a kidney that occurs following the removal of the opposite kidney. This was accomplished in dogs by enveloping the remaining kidney with strips of gauze, which were then

soaked with collodion and allowed to harden, a layer at a time, in situ. Such application of a cast to one kidney followed by extirpation of the opposite one is a reliable method of producing a pronounced and rapid rise in blood pressure. It is not clear, however, that the prevention of renal hypertrophy or active constriction of the kidney or its vessels is the active causative agent in these experiments.

Goldblatt, Kahn and Hanzel¹⁶ have studied the effect of constriction of the abdominal aorta above and below the origin of the renal arteries, and have concluded that the hypertension developing after constriction of the aorta above the origin of the renal arteries is of renal etiology. The findings of Page¹⁷ confirm this. Hypertension does not develop in dogs, however, if the aorta is constricted or occluded at the arch, a situation corresponding to that existing in man in the presence of coarctation of the aorta, a condition which is accompanied by hypertension. This difference is explained by the fact that in the dog extensive collateral circulation develops rapidly and with ease.

Taquini¹⁸ reports that on re-establishing the renal circulation after temporary occlusion of the renal arteries there is a rise in the arterial pressure. This hypertension is caused presumably by the liberation of a substance, formed in the totally ischemic kidney, that acts on the walls of the vessels throughout the body.

Significance should be attached to the publication of several reports on the biologic and chemical characteristics of the vasopressor and the vaso-depressor substances of renal origin. Corcoran and Page¹⁹ have found that renin (the vasoconstrictor substance extracted from the kidney of certain animals), when given slowly by intravenous injection to uninephrectomized dogs whose remaining kidney has been subcutaneously explanted, increases the systemic arterial pressure and the relative volume of renal glomerular filtrate while it decreases renal blood flow. The investigators suggest that this reduction of the blood flow depends on the constrictor effect of renin on the glomerular efferent arterioles. However, under different experimental conditions Steele and Schroeder²⁰ usually failed to observe any change in the renal blood flow following a single intravenous administration of renin. Subsequently Corcoran and Page²¹ reinvestigated this problem and found that the results substantiated their first conclusion that slow intravenous infusion of renin into uninephrectomized dogs with single explanted kidneys caused a decreased renal blood flow.

Page²² observed that after repeated injection of renin, a diminishing pressure response (tachyphylaxis) occurred in cats and dogs, even after the re-

removal of the liver, adrenal glands, kidneys or viscera. The pressor response to renin in brief experiments is independent of the height of the arterial pressure or of the presence of the adrenal glands. Evisceration and large doses of ergotamine reduce the response. The effect is largely uninfluenced by pithing, the intracisternal injection of renin, cocaine, strychnine and caffeine and the infusion of sodium bicarbonate or hydrochloric acid. No parallel was found between the pressor responses to renin on the one hand and to carotid-sinus stimulation, adrenalin and tyramine on the other. For a time, continuous infusion of renin produces a prolonged rise of arterial pressure in normal and in chronically adrenalectomized dogs, but eventually the pressure falls even though the injection is continued. Tachyphylaxis can develop in a rabbit's ear perfused with blood and small doses of renin, and the same blood perfused through a second ear will cause no vasoconstriction when renin is added. The addition of renin-activator restores the ability of renin to cause constriction. Renin alone causes no vasoconstriction when infused with Ringer's solution, but here again renin-activator restores activity. It is suggested that the diminishing pressor response observed in animals after repeated injection of purified renin is due to the loss of renin-activator and to the development of an "ant substance" in the blood. The vasoconstrictor effect of renin and renin-activator depends primarily on direct action on the blood vessels and is little influenced, at least in experiments of short duration, by the removal of the nervous system, endocrine glands and viscera. Page and Helmer²³ reported later on the chemical action of a crystalline pressor substance ("angiotonin") derived from the reaction between renin and renin-activator. The vasoconstrictor activity of purified renin can be restored by the addition of a protein-like substance contained in plasma and red blood cells (renin-activator). The activated renin, angiotonin, is a heat-stable, water-soluble, alcohol-soluble, fluorescent, and alkaline-labile substance. It is a reducing substance that is destroyed by strong oxidizing agents. It forms crystalline salts with oxalic and picric acids. Maximal amounts of angiotonin result when the proportion between renin and activator is roughly 3:100. Renin destroys angiotonin when incubated with it for a sufficient length of time. Angiotonin also has an activator—apparently different from the renin-activator—that can be separated from blood.

The purest preparation of renin elevates the arterial pressure 30 mm. of mercury in dogs, when injected in amounts representing 0.027 mg.

of nitrogen per kilogram of body weight. In cats it was three times as active. Color tests for guanidine groups and for pentose are especially strong in renin solutions; those for adrenaline are negative. Crystalline precipitates are formed by the addition of flavianic acid or picric acid to hydrolysates of renin. The pressor action of renin in cats and dogs is not abolished by ergotamine, nor potentiated by cocaine as is adrenaline. Cats, under Pentobarbital, are desirable animals for assay purposes.

Page and Helmer state that angiotonin causes marked contraction of intestinal segments of rabbits without reducing their rhythmic motion. It sensitizes the intestine to further doses of angiotonin and alters the intestine so that renin-activator contracts it. Angiotonin also constricts the vessels of a rabbit's ear perfused with blood or Ringer's solution. The kidneys form inhibitors to both renin and angiotonin.

Page²⁴ subsequently reported on the amount of renin, renin-activator and angiotonin-activator in the renal vein and in the arterial blood. Heparinized plasma derived from the blood of some patients with essential hypertension causes greater renin-activation than does normal human blood. Plasma from dogs with experimental hypertension also exhibits heightened power as compared with plasma of normal dogs. This, according to Page, suggests that the humoral mechanism in the two types of hypertension have much in common, and that in the hypertensive state there is either an increased amount of renin-activator in the blood or a decreased amount of renin-inhibitor.

Braun-Menendez, Fasciolo, Leloir and Munoz²⁵ report on the nature of the substance causing renal hypertension. Extracts of the venous blood from kidneys in acute ischemia contain a pressor substance ("hypertensin") that is also formed *in vitro* when blood proteins are incubated with renin. Some of the chemical and pharmacologic properties of hypertensin differ from those of other known substances. Renin is considered the enzyme, blood pseudoglobulins the substrate, and hypertensin the reaction product. Hypertensin disappears if the reaction is permitted to go too far, and is also inactivated by other proteolytic enzymes and by blood. The pressor action of renin appears to be due to the formation of hypertensin in blood, and a similar mechanism is suggested for arterial hypertension due to renal ischemia.

Pickering and Prinzmetal²⁶ report on the nature of diuresis induced in the rabbit by renin. The intravenous dose of renin necessary to produce diuresis in the anesthetized rabbit is greater than that needed to produce a rise in arterial pressure. In

the unanesthetized rabbit under special experimental conditions, renin can have an antidiuretic effect, which is attributed to its action on the glomerular vessels in reducing the rate of glomerular filtration. The diuretic effect of renin in the unanesthetized rabbit is due to an inhibition of tubular reabsorption of water, sodium and chloride. This may represent the effect of a pressure diuresis in which relatively few nephrons are involved, but it is more probably due in part to the direct action of renin on the function of the renal tubule cells.

Williams, Grollman and Harrison²⁷ found that an extract of the kidney, administered before the renin, diminished its pressor effect, and that such extracts also reduced the blood pressure of rats with hypertension due to removal of renal tissue. Likewise, in hypertensive dogs treated with renal extracts, the blood pressure was appreciably reduced, normal values being attained in some cases. Oral administration of extracts to normal animals did not produce a decline in blood pressure. Unless the hypertension was mild, several untoward symptoms and even death were associated with the decline of pressure. Grollman, Williams and Harrison²⁸ have treated a small number of patients by means of oral or parenteral administration of the renal antipressor substance. In most of the subjects, it is claimed, a decline in the blood pressure occurred. The renal antipressor substance apparently has certain unique properties that differentiate it from various depressor tissue extractives described previously by investigators. This depressor substance is still very costly and difficult to obtain. In the discussion of the above reports Winternitz²⁹ stated that the crude ammonium sulfate preparation of renin contains pressor and depressor substances, as well as agents that necrotize certain muscles, including the heart muscle, the smooth muscles of the arteries, veins and other hollow muscular viscera, and diaphragmatic but not skeletal muscle. Renin D, according to Winternitz, contains three ferments: a tryptic, a peptic and a catalytic type. At the same meeting Jablons³⁰ reported that he had treated hypertensive animals and patients with a hypotensive, protein-free, aqueous, acid-alcohol extract. Some of the patients reacted well, whereas others were not benefited.

The interpretation of these results bearing on the nature of pressor and depressor substances and on their biologic significance in disease is difficult.

TREATMENT

There has been no significant progress in the treatment of arterial hypertension and its complications. However, advances in the knowledge

of the pathogenesis and treatment of pyelonephritis bear significantly on the prevention of hypertension due to chronic or healed pyelonephritis. Similarly the demonstration that within a period of weeks toxemia of pregnancy can induce structural changes in the renal vessels suggests that timely interruption of toxemic pregnancies will reduce the tendency to post-toxemic arterial hypertension.

The present status of the treatment of arterial hypertension and its complications, including a review of the recent literature on the subject, have been discussed elsewhere. It has been pointed out that a diet low in sodium (salt) is neither practical nor very effective in the treatment of essential hypertension or hypertension caused by chronic pyelonephritis. In the toxemias of pregnancy (pre-eclampsia and eclampsia) and in many cases of acute or subacute glomerulonephritis, on the other hand, a low-sodium intake not only improves the degree of edema, but also lowers the arterial pressure. Recently, by claiming the regime efficacious, Martini³² and Kampmann³³ revived the interest in a rigid salt-free diet combined with periodic fasting in the treatment of arterial hypertension. The initiation of the fasting period is preceded by saline laxative. During the eight days of fasting usually about 750 cc. of fruit juices or tomato juice are given daily. One cup of tea or a small amount of fresh fruit or salad may be added. No other fluids are allowed. About three days after the end of the strict fasting period the patient returns to the salt-free diet. During the transition period potato, vegetables, salads and applesauce are added to the diet. The report suggests that this strict diet is not without danger. It should be carefully supervised in old persons, and in the presence of severe heart failure and myocardial infarction it is contraindicated. Depression, nervousness and weakness have occurred in some patients on this regime. A tendency to circulatory collapse developed in others.

The use of the depressor substance of renal origin, as recommended by Grollman, Williams, and Harrison,²⁸ is still in the experimental stage, and the drug is both costly and difficult to obtain. For these reasons it is too early to express an opinion on the drug's significance from a therapeutic point of view.

The therapeutic value of neurosurgical procedures is still an unsettled question. Smithwick³¹ reports on his surgical experience in approximately 150 cases of hypertension. He believes that sympathectomy yields its best result when the operation is adequately complete, preganglionic in type and extensive enough to guard against future regeneration of interrupted pathways. If the splanchnic

nic area was thoroughly denervated, an immediate postural change in blood pressure resulted in every case. Under these circumstances the blood-pressure level in all positions and the pulse pressure were lower than before operation. If splanchnic denervation is less complete, and if no significant postural change is noted, there is usually no significant change in the blood pressure level in any position, particularly in the more advanced stages of the disease. Apparently, a few uninterrupted fibers are capable of supplying enough tone to the splanchnic area so that no significant change will occur in blood pressure after operation.

According to Smithwick, removal of virtually the entire great splanchnic nerve and division of all its aortic branches, coupled with interruption of the communicating rami of the ninth, tenth, eleventh and twelfth dorsal and first lumbar segments, and with excision of the sympathetic trunk over this area, constitute the minimal procedure that has been found consistently to produce the blood pressure change described above. Whether removal of the outflow from the second lumbar segment is also desirable has not been determined. Smithwick considers his contribution as a preliminary report, and he emphasizes that it will take several years to ascertain the value of this procedure in the treatment of hypertension.

If one recalls the number of claims and counterclaims as to the efficacy of the numerous types of neurosurgical procedures ever since Pieri²⁵ in 1932 resected both splanchnic nerves in patients with essential hypertension, one wonders about the effectiveness of these measures. Volini and Flaxman,³⁰ impressed by the observation that the majority of proposed therapeutic measures have a brief popularity and then pass into obscurity, undertook a comparative evaluation of the results of nonspecific surgical measures (hysterectomy, cholecystectomy and prostatectomy) and of specific neurosurgical operations (extensive sympathectomy, splanchnic nerve resection and celiac ganglionectomy). The authors followed the effects of fifty-two operations on hypertensive patients and concluded that any of the claims made for the efficacy of specific operations can likewise be made for nonspecific surgical measures. Obviously, then, the value of neurosurgical treatment of hypertension is not yet established.

721 Huntington Avenue

3 Stead E A Jr and Kunkel P The nature of peripheral resistance in arterial hypertension *J Clin Invest* 19 25-33 1940
4 Hines E A Jr The significance of vascular hyperreaction as measured by the cold pressor test *Am Heart J* 19 408-416 1940
5 Miller J H and Bruger M The cold pressor reaction in normal subjects and in patients with primary (essential) and secondary (renal) hypertension *Am Heart J* 18 379-383 1939
6 Thomas C B and Warthin T A The response of normal dogs and dogs with experimental hypertension to a standard cold stimulus *Am Heart J* 19 316-319 1940
7 Weiss S Dexter L Parker F Jr and Tenney B Jr Arterial hypertension in pregnancy and the hypertensive toxemia syndrome of pregnancy (pre-eclampsia and eclampsia) *Tr Am Physicians* 55 282-288 1940
8 Schroeder H A and Steele J M Studies on essential hypertension. I. Classification *Arch Int Med* 64 927-951 1939
9 Williams J R Jr and Harrison T R Clinical pictures associated with increased blood pressure: a study of one hundred patients *Ann Int Med* 13 650-670 1939
10 Weiss S The clinical and physiologic characteristics of arterial hypertension. *Diagnosis and Treatment* Ed by Forest R Moulton 331 pp Washington American Association for the Advancement of Science 1940 P 300
11 Rosenthal E I The brain in malignant hypertension: a clinicopathologic study *Arch Int Med* 65 545-586 1940
12 Stead E A Jr and Kunkel P Mechanism of arterial hypertension induced by Parealol (p-hydroxyphenethylamine) *J Clin Invest* 18 439-448 1939
13 DeWesselow O J V S and Thomson W A R A study of some serum electrolytes in hypertension *Quart J Med* 8:361-374 1939
14 Page I H The production of persistent arterial hypertension by celophane pericapsitis *J A M A* 113 2046-2048 1939
15 Greenwood W G Nassim R and Taylor N B The production of hypertension by the prevention of kidney hypertrophy *Canad Med J* 41 443-445 1939
16 Goldblatt H Kahn J R and Hanzel R F Studies on experimental hypertension. XI. The effect on blood pressure of constriction of the abdominal aorta above and below the site of origin of both main renal arteries *J Exper Med* 69 649-674 1939
17 Page I H The effect of chronic constriction of the aorta on arterial blood pressure in dogs: an attempt to produce coarctation of the aorta *Am Heart J* 19 218-237 1940
18 Taqui N A C The production of a pressor substance by the totally ischemic kidney *Experientia* 19 513-518 1940
19 Corcoran A C and Page I H The effects of renin on renal blood flow and glomerular filtration *Am J Physiol* 128 795-797 1940
20 Steele J M and Schroeder H A Effect of renal extract (renin) upon the flow of blood through various organs *J Clin Investigation* 18 47-1029
21 Corcoran A C and Page I H Effects of renin, pituitrin and pressin on renal blood flow and clearance *Am J Physiol* 116 354-367 1939
22 Page I H On the nature of pressor action of renin *J Exper Med* 70 571-577 1939
23 Page I H and Hemer O M Crystalline pressor substance (angiotensin) resulting from the reaction between renin and renin activator *J Exper Med* 71 79-87 1940
24 Hemer O M and Page I H Purification and some properties of renin *J Biol Chem* 127 757-763 1939
25 Page I H Demonstration of the location of renin in the blood stream in kidneys of animals made hypertensive by celophane pericapsitis *Am J Physiol* 130 27-28 1940
26 Dieren C Effect of normal and hypertensive plasma on intestinal segments treated with renin *Idid* 10 29-33 1940
27 Braun Menendez F Fasciolo J C Leloir L F and Munoz J M The substance causing renal hypertension *J Physiol* 93 783-788 1940
28 Packer G W and Prinzmetal M The effect of renin on urine formation *J Physiol* 93 314-335 1940
29 Harrison T R Grollman A., and Williams J R Jr The antipressor action of renal extracts and their capacity to reduce the blood pressure of hypertensive rats. *Am J Physiol* 128 17-24 1940
30 Williams J R Jr Grollman A. and Harrison T R The reduction of the blood pressure of hypertensive dogs by the administration of renal extract *Am J Physiol* 130 495-507 1940
31 Grollman A., Williams J R Jr, and Harrison T R Reduction of elevated blood pressure by administration of renal extracts *J A M A* 115 1169-1176 1940
32 Winterstein M C Discussion of Grollman, Williams and Harrison²⁹
33 Johnson B Discussion of Grollman, Williams and Harrison²⁹
34 Weiss S Arterial hypertension and its complications. In *Modern Medical Therapy in General Practice* Edited by David P East Vol III 1116 pp Baltimore W Williams & Wilkins Co 1940 Pp 2711-2749 Diet and Bright's disease. *Connecticut State J (in press)*
35 Martini P Ueber die Behandlungsmöglichkeiten des genuine Hochdrucks insbesondere unter salzreicher Ernährung *Monatshchr* 15 1409-1414 1935
36 Kampmann W Ueber die Behandlungsmöglichkeiten des Hochdrucks insbesondere über das Fasten *Deutsches Arch f Klin Med* 184 216-231 1937
37 Smithwick R H A technique for splanchnic resection for hypertension *Am J Surg* 71 18-19 1940
38 Pieri G Tentative di cura chirurgica dell'ipertensione arteriosa *Chirurgia* 43 1173-1182 1932
39 Volini I and Flaxman N The effect of nonspecific operations on essential hypertension. *J A M A* 112 2126-2128 1937

1 Robinson S C and Brucer M Range of normal blood pressure: statistical and clinical study of 11383 persons *Arch Int Med* 64 409-444 1940
2 Asman D. and Goldshine A D Blood pressure determinations by patients with essential hypertension *Am J M Sc* 200-465-474 1940

CLINICAL DIAGNOSIS

Osteomyelitis of the tibia.

DR. SIMMONS'S DIAGNOSIS

Metastatic tumor?

Osteogenic sarcoma?

ANATOMICAL DIAGNOSIS

Osteogenic sarcoma of the tibia.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: The differential diagnosis on the ward was essentially the same as that of Dr. Simmons. They felt that the odds were against an inflammatory lesion and in favor of tumor. They were not very anxious to commit themselves as to the nature of the tumor.

She was explored and a tumor found, and an amputation was performed. The tumor was a spindle-cell sarcoma producing very little bone, but I think one has to classify it either as an osteogenic sarcoma or a periosteal fibrosarcoma. The extensive bone destruction, the new-bone formation, albeit slight, and the numerous tumor giant cells incline me to the diagnosis of osteogenic sarcoma, however. It certainly is not a reticulum-cell sarcoma. The tumor had destroyed almost the whole lower third of the tibia. It had extended down to the cartilaginous plate at the lower end but had not broken through, the latter remaining as a firm shell between the tumor and the joint. The tumor spread out into the surrounding soft tissues and completely encapsulated the tibia.

CASE 26492

PRESENTATION OF CASE

A seventy-year-old single woman entered the hospital after coughing or vomiting a large quantity of blood.

Because of the patient's disorientation, the history was obtained from relatives. It appeared that she had been short of breath for a number of years, and four months before admission had spent ten weeks in another hospital because of a coronary occlusion. Following this incident she developed pleurisy, but no details of this illness could be obtained. For some years the patient had suffered from indigestion and for several months before entry had complained of many vague pains, including one in the abdomen that was unrelated to food or activity, but was accompanied by anorexia. Her physician had treated these symptoms with sedatives. During the two weeks prior to entry, she had been disorientated, and it was noticed that her

stools were tarry. One week later she developed a nonproductive cough, and four days later swelling of the ankles. On the day of admission she brought up a mouthful of bright-red blood and on two occasions, shortly afterward, dark blood clots. The patient had been losing weight for a year and in the last few weeks before entry had "seemed to melt away."

The patient had had "three nervous breakdowns" in her youth. One brother had died of cancer of the prostate.

Physical examination showed an undernourished, frail woman, who appeared acutely and chronically ill. She lay moaning and muttering and was considerably disorientated. The skin was pale, dry and wrinkled; small, soft lymph nodes could be felt in the neck and axillas; the breasts were normal. Respirations were rapid and shallow, but the lungs were clear. The heart was slightly enlarged and regular, with a loud systolic murmur over the entire precordium; the blood pressure was 116 systolic, 60 diastolic. The abdomen was tense, but no masses or viscera were palpated. Rectal examination was negative; the vaginal introitus was virginal. There was pitting edema of the ankles, and slight varicosities of the legs.

The temperature was 98°F., the pulse 100, and the respirations 20.

Examination of the urine was negative. Examination of the blood showed a red-cell count of 3,500,000 with a hemoglobin of 52 per cent, and a white-cell count of 7900. There was a marked variation in size and shape of the red cells. The non-protein nitrogen of the blood serum was 26 mg. per 100 cc., the protein 4.5 gm., the carbon dioxide combining power 26.9 milliequiv. per liter, and the chlorides 101.8 milliequiv. Five stool examinations were tarry and guaiac positive.

X-ray examination of the chest showed the left diaphragm to be slightly higher than usual, with clear costophrenic angles. The heart was enlarged on both sides; the aorta was tortuous, dilated and calcified. The bones showed a generalized decalcification. With a gastrointestinal series the esophagus appeared normal, and the stomach contained a moderate amount of foreign material that could possibly have been blood. There were no gross filling defects or ulcerations, and the duodenum showed no evidence of disease. There was extensive calcification in the abdominal aorta.

An electrocardiographic recording showed normal rhythm, a low T₁, diphasic T₂ and T₃, a mostly inverted and diphasic T₄, and a probably absent R₄. The PR interval was 0.12 second.

The patient was put on a gastric diet, and vomiting did not recur until the sixth hospital day,

when it was associated with epigastric tenderness. The vomitus did not contain blood. The lungs were clear. Three days later, 50 cc. of green guaiac-negative fluid was removed from the stomach, and the pain and distention that had developed were relieved by an enema. The patient complained continually of abdominal pain, but examination never revealed more than a generalized tenderness. There was no spasticity. Despite supportive measures, including one transfusion of 500 cc. of blood, the patient failed rapidly and died two weeks after admission.

DIFFERENTIAL DIAGNOSIS

DR. ALLEN G. BRAILEY: The patient was already so sick when she reached the hospital that it was not possible to get really adequate information about her. The history is incomplete and may be inaccurate; several laboratory studies would probably have been done if her condition had been more satisfactory. In trying to decide what was the cause of death, let us first consider what kind of illness she had, whether acute or chronic.

We are told that for several years she had had indigestion and shortness of breath; for one year she had been losing weight; for a few months she had had abdominal pain and anorexia; for two weeks she had had tarry stools; and in the hospital she failed rapidly. In other words, she seems to have had a chronic illness that began rather vaguely several months before admission, steadily gaining momentum to the time of its termination. To be sure, it was punctuated by episodes such as the coronary occlusion and the attack of pleurisy, which I assume to have been due to an embolus dislodged from the right ventricular wall. But there is little suggestion in this history of the dramatic change of events that characterizes acute disease.

We may approach this problem from another angle and ask where the disease process was located. We may mention the urinary tract only to rule it out. The nonprotein nitrogen was 26 mg. per 100 cc., and we have the laconic statement that the urine was normal. In fact none of the evidence implicates the kidneys or bladder. Similarly, the respiratory tree seems a most unlikely locus. It is possible to swallow a good deal of bronchial secretion. Indeed, in pulmonary tuberculosis, examination of the stomach contents often yields more tubercle bacilli than does the sputum. But this patient could not have swallowed enough blood from the lungs to produce tarry stools for two weeks. Can the disease process have been primary in the cardiovascular system? The arteries were certainly very sclerotic, as evi-

denced by the x-ray picture of the aorta, by the history of coronary occlusion and by her mental status, which I assume was due to arteriosclerosis of the cerebral vessels aggravated by anemia. Could the hemorrhage have arisen from rupture of an aneurysm into the gastrointestinal tract? The abdominal pain, perhaps, ought to raise the question of dissecting aneurysm. But the pain was too mild; it lasted too long; and no evidence developed of the arterial shutoff to kidneys or legs that is common in dissecting aneurysm of the aorta. Dissecting aneurysm is preceded by hypertension. This woman might well have had hypertension before the cardiac infarction, but she probably had had little since. I should think that dissecting aneurysm would rarely occur after one's blood pressure has been lowered by any such myocardial injury. There can be little doubt that the fatal disease lay in the gastrointestinal tract.

DR. AUBREY O. HAMPTON: They apparently were not very interested in this patient's stomach or duodenum, as judged from the number of films that were taken and from the report. Apparently it was a routine, negative fluoroscopy. They did look for varices in the esophagus and did not find them. In examining the stomach they were handicapped by what was presumed to be foreign material. If these filling defects moved, they were foreign material; but if they did not, they might have been due to a tumor. I do not see any evidence of tumor here.

These shadows near the fundus look like enlarged mucosal folds, and in an elderly woman with cachexia and without hypertension, the folds should be small and atrophic.

She did have an enlarged heart. This is not the true size, however, since this is a portable or "back-to" film, and the size of the heart and aorta is exaggerated.

DR. BRAILEY: Do you think the duodenum was all right?

DR. HAMPTON: This is a normal-looking duodenal cap. The abdominal aorta shows extensive calcification all the way; it is not dilated.

DR. BRAILEY: Did she bleed from esophageal varices? The negative x-ray examination does not exclude that possibility. But we have no evidence of hepatic cirrhosis, and the blood smear is that of long-standing anemia, which, if due to hemorrhage, must be caused by chronic rather than acute blood loss. The hemorrhage from varices is apt to be a succession of acute and widely spaced blood lettings. Could the blood have come from below the duodenum? In the literature there are reports of reverse peristalsis so violent that enemas

had to be stopped because the patient complained of the taste of the enema fluid, but such reversal of flow is uncommon except in intestinal obstruction. On the day of admission the patient brought up bright-red blood that could hardly have come from much below the stomach. The diagnosis that best fits this history is carcinoma of the stomach, with hemorrhage therefrom.

DR. WILLIAM B. BREED: Dr. Hampton, from the x-ray films are you willing to make a diagnosis of hypertrophic gastritis?

DR. HAMPTON: No. I am assuming that the irregularities were due to large folds that are inadequately demonstrated. To be sure that they are present, one must fluoroscope the patient. These defects are the only abnormal finding I can see in the films that we have.

DR. BREED: We know that hypertrophic gastritis may give massive bleeding such as this. I do not believe it can be entirely excluded.

DR. BRAILEY: I thought about gastritis. The patient was very sclerotic, and the symptoms and downhill course could have been due to senility and circulatory changes in the stomach. But it is a quite impressive picture of rapidly advancing cachexia, which I think was more likely due to cancer than to old age and gastritis.

CLINICAL DIAGNOSES

Carcinoma of the stomach.
Coronary heart disease.

DR. BRAILEY'S DIAGNOSIS

Carcinoma of the stomach.

ANATOMICAL DIAGNOSES

Acute gastritis.
Arteriosclerosis, generalized.
Coronary occlusion, old.
Infarct of the heart, healed.
Pulmonary infarcts.
Thrombosis, left popliteal vein.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: The post-mortem examination showed an area — about 6 cm. in diameter — of very shallow erosion and hemorrhage in the stomach that we must call acute gastritis, although certainly not a hypertrophic gastritis, because the rugae were thin rather than thick. There was nothing else in the gastrointestinal tract. There were severe generalized arteriosclerosis, including the coronary arteries, and an old infarct of the heart in the left ventricle, with an overlying thrombosis. There was an infarct in the lung, and the source of the embolus, as in probably nine out of ten cases, was an unsuspected thrombosis in the popliteal vein.

The brain showed atrophy and rather diffuse arteriosclerosis of the vessels at the base, but no visible or palpable areas of softening. I do not think we can make out a case here for Cushing's syndrome of gastric erosion secondary to a cerebral lesion.

The New England Journal of Medicine

Formerly the

Boston Medical and Surgical Journal

Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE
ON PUBLICATIONS

Official Organ of

THE MASSACHUSETTS MEDICAL SOCIETY
THE NEW HAMPSHIRE MEDICAL SOCIETY
THE VERMONT STATE MEDICAL SOCIETY

EDITORIAL BOARD

Joseph Garland M.D.	John P. Sutherland M.D.
William B. Breed M.D.	Stephen Rushmore M.D.
George R. Minot M.D.	Henry R. Vetus M.D.
Frank H. Lahey M.D.	Robert M. Green M.D.
Sheldon Warren M.D.	Charles C. Lund M.D.
George L. Tobey Jr. M.D.	John F. Fulton M.D.
C. Guy Lane M.D.	A. Warren Searns M.D.
William A. Rogers M.D.	Dwight O'Hara M.D.

ASSOCIATE EDITORS

Thomas H. Lanman M.D.	Donald Munro M.D.
Henry Jackson Jr. M.D.	

Walter P. Bowers M.D. EDITOR EMERITUS
Robert N. Nye M.D. MANAGING EDITOR
Clara D. Davies ASSISTANT EDITOR

SUBSCRIPTION TERMS: \$5.00 per year in advance (postage paid for the U.S. and States); Canada \$5.04 per year; \$5.52 per year for all foreign countries (postage paid for the U.S. and States); \$5.52 per year for all foreign countries (postage paid for the U.S. and States).

TERMINAL: For early publication should be received not later than noon on Friday.

THE JOURNAL does not hold itself responsible for statements made by any contributor.

COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston, Massachusetts.

SPECIALISM ITS DANGERS

If the specialist in medicine is merely the physician who by long and arduous training has acquired knowledge and skill to an unusual degree how can there be any danger? Is not specialism the very foundation of progress in the science and art of medicine, the only way by which the boundaries of knowledge can be extended? For the human, however, dangers do exist, particularly since there is no statutory definition of specialism or the specialist, and any physician can legally apply the latter designation to himself.

What constitutes a specialty? Certainly not the mere designation of the part of the body to be treated. The qualified physician or general practitioner may treat the mind or any part of the

body, no matter how many specialists claim it as their own. Yet one danger from specialism is that physician and layman may come to think that no one but a specialist is competent to practice in any field.

Another danger is that the qualified specialist may look at medicine with a microscopic eye and, of necessity, see only his chosen field, and that out of perspective. Then he may be inclined to think that the cause of all bodily ills—such as bad posture, eyestrain and indigestion—lies in his field.

But the most serious dangers arise because of the existence of the unqualified, self-designated "specialist." A little detailed knowledge may give him undue confidence so that he undertakes what is far beyond his competence. He may claim for himself what he does not possess. He may say that he is a specialist because he wants to be known as such, and because he wants to derive whatever benefit may come from such a designation. The danger at this point is substantially the danger from misrepresentation. It is not that a physician should not practice in a special field, but the claim that he is qualified when he is not.

Perhaps there should be a change in the statute, a designation there as deceit, if proper qualification for the claim to be a specialist is not shown. The difficulty then will be to determine what should be required so that a physician may properly be known and practice as a specialist. The difficulty is not insuperable, but it is clear that a man's claim for himself that he is a specialist should not be the only criterion for qualification.

SMALLPOX

Of all the communicable diseases that have scourged mankind, the one that has been immunologically preventable for the longest time and on the whole most satisfactorily is smallpox. It is a reflection on the effectiveness of our particular form of democracy, desirable is that political condition may otherwise be that India alone has a higher smallpox rate than the United States.

Perhaps we should congratulate ourselves that the year 1939, according to a recent issue of the *Statistical Bulletin* of the Metropolitan Life Insurance Company, registered an improvement over 1938, a drop from 14,983 cases to only 10,059 — of an entirely unnecessary disease! Even with this decrease, the annual average of 9563 cases for the preceding five years is still exceeded.

The smallpox belts of the United States consist of the north-central states and those lying west of the Mississippi River — sections, apparently, where personal liberty still bulks larger, in some particulars, than does the common good. A number of these states showed a rise in smallpox incidence — notably Ohio, Indiana, Michigan, Iowa, Oklahoma and Tennessee; other records on the wrong side of the ledger were chalked up against California, Texas, Illinois and Washington. We may reasonably point with pride to the fact that the six New England states and New Jersey, Pennsylvania, Delaware and Maryland, with a combined population of over 25,000,000 have reported a total of 14 cases since 1933.

Vaccination has unfortunately been accepted for years by a vociferous group as a symbol of the loss of individual liberty. How dearly such liberty can be bought will be discovered by the north-central and western states if the present mild type of smallpox suddenly develops into the virulent variety.

MEDICAL EPONYM

AUSTIN FLINT MURMUR

Austin Flint (1812-1886), then professor of the principles and practice of medicine in the Bellevue Hospital Medical College, New York City, first fully described this murmur in a paper, "On Cardiac Murmurs," which appeared in the *American Journal of the Medical Sciences* (N.S. 44:29-54, 1862).

Now in cases of considerable aortic insufficiency, the left ventricle is rapidly filled with blood flowing back from the aorta, as well as from the auricle, before the auricular contraction takes place. The distension of the ventricle is such that the mitral curtains are brought into coaptation, and when the auricular contraction takes place the mitral direct current passing between the curtains throws them into vibration and gives rise to the characteristic blubbery murmur. The physical condition is in effect analogous to contraction of the mitral orifice from an adhesion of the curtains at their sides, the latter condition, as clinical

observation abundantly proves, giving rise to a mitral direct murmur of a similar character.

A mitral direct murmur, then, may exist without mitral contraction and without any mitral lesions, provided there be aortic lesions involving considerable aortic regurgitation.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

RAYMOND S. TITUS, M.D., *Secretary*
330 Dartmouth Street
Boston

TOXEMIA OF PREGNANCY, ASSOCIATED WITH DIABETES AND RESULTING IN INTRAUTERINE DEATH

Mrs. R., a thirty-one-year-old para III with diabetes of eleven years' duration, was first seen on August 3, 1939, when she was approximately eleven weeks pregnant.

The family history was noncontributory. The patient's past history included, in addition to the diabetes, scarlet fever and measles. She had undergone a tonsillectomy and a sinus operation. Catamenia began at sixteen, were regular with a twenty-eight-day cycle and lasted two to three days. The last period began on May 13, making the expected date of confinement, February 25, 1940. The first pregnancy occurred in 1936, when the patient was delivered of a full-term, macerated fetus that was said to be "big." The second pregnancy, in 1937, ended in a spontaneous abortion at approximately ten weeks; the patient was cured.

Physical examination on August 3 revealed a very short, stocky woman. The weight was 103 pounds, the height 4 feet, 9 inches. The heart was not enlarged; there were no murmurs. The lungs were clear and resonant; there were no rales. The blood pressure was 140 systolic, 70 diastolic. The fundus was palpable by abdominal examination. Vaginal examination revealed the cervix to be posterior, the fundus anterior.

The patient was seen continuously by her obstetrician and a specialist in diabetes. During the twenty-first week the blood-prolan level rose, and the administration of stilboesterol and Pregnenolone was begun. It remained elevated during the twenty-third, twenty-fifth, twenty-eighth, twenty-ninth, thirty-third, thirty-fourth, thirty-fifth, thirty-sixth and fortieth weeks, fluctuating between 200 and 500 rat units per 100 cc.

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

On January 30 the patient entered a hospital because of blurred vision and a blood pressure of 140 systolic. On February 12 she was examined vaginally, and the cervix was found to be almost ready for induction. It was decided to induce labor the next week. On February 17 she was transferred to another hospital, and labor started spontaneously about 9:30 p.m. The membranes ruptured at 9:45 p.m. By 11:00 p.m. the cervix was fully dilated, with the head on the perineum. The head was delivered normally, the body with much difficulty. Although it was said that the fetal heart was heard five hours before delivery, the fetus was macerated. It weighed 9 pounds, 14 ounces.

A few days after delivery, the patient was transferred to the hospital she had entered on January 30, where, unfortunately, she was placed in a ward in which there was sepsis. Two days later, following a chill, the temperature rose to 103°F., the pulse to 120. A culture from the uterus showed hemolytic streptococci, and the patient was given sulfanilamide, with almost immediate marked improvement. She was discharged in good condition on March 3.

Comment. This patient was a very small woman whose normal weight was about 100 pounds. The first pregnancy illustrates the frequent phenomenon of a large child born at term in a macerated state. The second pregnancy resulted in spontaneous abortion, a complication that was frequently met with before the discovery of insulin and that still occurs. The third pregnancy progressed quite satisfactorily. Blood examination revealed a high prolactin early in pregnancy, and the oral administration of stilboesterol and Pregneninolone was instituted; however, the level of the prolactin was not controlled, and the patient developed definite clinical signs of toxemia — an elevated blood pressure, blurred vision, edema, and albumin in the urine. It is possible, however, that the therapy succeeded in keeping this toxemia in abeyance, because the patient was at no time clinically ill.

The patient was allowed to go nearer the end of expected confinement than she would have been a few years ago. The labor was very simple; the delivery of the head was easily accomplished, but the size of the thorax and chest made the rest of the procedure difficult. Several observers stated that they heard the fetal heart five hours before delivery, and there is also a note stating that it was audible not long before delivery; yet the fetus was born in a state of beginning maceration. It is fair to infer that if this baby had been delivered a week or ten days earlier, or had the hormonal therapy been adequate, it would have been born alive and would probably have survived,

since its weight at birth was 9 pounds, 14 ounces.

Until live babies are born at term in diabetic patients suffering from toxemia that has been diagnosed by the blood-prolactin level and treated by sufficient doses of estrogens and progestins, it is still a tenable dictum, so far as the infant's survival is concerned, to empty the uterus at or about the thirty-seventh week of pregnancy.

A secondary complication was the hemolytic streptococcus infection, which was undoubtedly picked up on the ward. The treatment with sulfanilamide and its rapid curative effect illustrate the value of chemotherapy in obstetrics.

COMMITTEE ON INDUSTRIAL HEALTH

CHARCOT JOINT AND TABOPARESIS

Viewed from an industrial standpoint the following case of syphilis is of interest.

The patient, a forty-two-year-old screw-machine operator, was a diligent, fast worker but never particularly accurate. During his period of intermittent employment from 1928 to 1940 he had had two physical examinations at the factory dispensary, both of which were essentially negative. In June, 1940, a third examination was negative except for positive Kahn and Hinton tests on blood samples.

In early July, 1940, he did not report for work and was said to be under treatment for "sciatica" by his family physician. On July 22 he appeared at the company dispensary with the following story: For the past five weeks he had been unable to work because of pain and disability of the left hip and thigh. The patient walked with a marked hip limp. Examination showed that the left thigh was 5 cm. larger than the right, and the left leg was approximately 4 cm. shorter than the right. Motions of the left hip joint were surprisingly good and appeared to be more restricted by swelling than by joint disease. The knee jerks were absent. The patient was sent to Worcester City Hospital for study and treatment. An abstract of the hospital record follows:

On admission, July 23, the patient complained of shortening in left hip and difficulty in walking of 3 weeks' duration.

For the past 3 or 4 years the patient had experienced occasional shooting knife-like pains down his legs, which he thought were due to "neuralgia." His general health had been good, and he had worked regularly. Four weeks before entry, he developed a peculiar numbness in the region of the left thigh, and he thought the part was somewhat swollen. A week later, while he was walking downtown, he suddenly, without apparent cause, developed a limp. He felt "as if something let go," and the left leg became shorter than the right. He could bear his weight, but to do so was painful at times; the limp persisted. From then on he was confined at home most of the time, and medicine furnished by his physician had given no

relief. The thigh was swollen but not especially tender; with certain positions or motions, however, he experienced acute excruciating pain in the region of the left hip joint.

Physical examination was essentially normal except for the extremities. The left thigh was regularly swollen, and there was somewhat firm, limited tenderness over the hip joint. The overlying skin was reddened, and the surface temperature seemed to be increased. The diameter of the thigh was roughly 5 cm. greater than that of the right thigh. The left leg was at least 2.5 cm. shorter



FIGURE 1.

than the right. There was fair voluntary control of the leg, but motion was limited by the swelling and underlying lesion. No knee jerks or ankle jerks were obtained; there was no Babinski sign or clonus. Sensation was preserved. A few small inguinal lymph nodes were palpable. The admission diagnoses were as follows: syphilis; gumma (?); sarcoma (??).

Urine analyses were negative. The red-cell count was 4,100,000 with 75 per cent hemoglobin, and the white-cell count 9400. The blood sugar was 90 mg. per 100 cc.; the nonprotein nitrogen, 37 mg.; the phosphatase 13.4 units; the phosphorus, 3 mg.; the calcium 8 mg. The blood Hinton and Kahn tests were positive. A clear specimen of spinal fluid contained 94 cells per cubic millimeter, of which 76 were lymphocytes and 10 polymorphonuclears; the Wassermann test was strongly positive; the gold-sol test was 5432221100; the total protein was 65 mg. per 100 cc.

On x-ray examination there was almost complete destruction of the head and neck of the left femur and some bone debris in the region of the joint (Fig. 1). There was a questionable lesion in the upper portion of the left ilium. The lesion in the left hip was thought to be consistent with a Charcot joint, but malignant tumor could not be ruled out. Re-examination was advised, and stereoscopic films showed a typical Charcot joint, with

complete destruction of the head and neck of the femur and some destruction in and around the acetabulum.

The patient was irritable and troublesome at times, and euphoric and bombastic at others. A neurologist believed that the patient had taboparesis. The patient was discharged, unimproved and against advice, on August 1. The discharge diagnoses were as follows: Charcot joint, left hip; taboparesis.

The interesting features of this case are the rather sudden onset, the worker's ability to walk with a very severe hip lesion and the fact that his mental condition did not cause a falling off in his earnings up to the time of stopping work. It also shows the value of routine blood examinations of all employees.

MEDICAL POSTGRADUATE EXTENSION COURSES

The following sessions, given by the Massachusetts Medical Society in co-operation with the Massachusetts Department of Public Health, the United States Public Health Service and the Federal Children's Bureau, have been arranged for the week beginning December 9:

BARNSTABLE

Sunday, December 15, at 4:00 p.m., at the Cape Cod Hospital, Hyannis. Obstetrical Complications with Case Histories and Clinical Problems. Instructor: John Rock. Donald E. Higgins, *Chairman*.

BRISTOL NORTH

Thursday, December 12, at 4:00 p.m., at the Morton Hospital, Taunton. Technique and Treatment of Primary, Secondary and Tertiary Syphilis. Instructor: William P. Boardman. Lester E. Butler, *Chairman*.

BRISTOL SOUTH (New Bedford Section)

Friday, December 13, at 4:00 p.m., at St. Luke's Hospital, New Bedford. Operative Obstetrics: Indications and technic. Instructor: Roy J. Hefernan. Robert H. Goodwin, *Chairman*.

ESSEX NORTH

Friday, December 13, at 4:30 p.m., at the Clover Hill Hospital, Lawrence. Therapeutic Uses of Preparations of Endocrine Glands. Instructor: Marshall N. Fulton. John Parr, *Chairman*.

ESSEX SOUTH

Tuesday, December 10, at 4:00 p.m., in the Conference Room, Salem Hospital, Salem. Recent Advances in Medical Therapeutics. Instructor: G. Philip Grabfield. J. Robert Shaughnessy, *Chairman*.

MIDDLESEX NORTH

Friday, December 13, at 5:00 p.m., at St. John's Hospital, Lowell. The Treatment of Varicose Veins. Instructor: Edward A. Edwards. William S. Lawler, *Chairman*.

PLYMOUTH

Tuesday, December 10, at 4:30 p.m., in the Nurses' Home of the Brockton Hospital, Brockton. Diagnosis and Treatment of Minor Lesions of Rectum and Anus. Instructor: Franklin G. Balch, Jr. Walter H. Pulsifer, *Chairman*.

RESOLUTION ON THE DEATH OF DR EDMUND FRANCIS WALSH

Edmund Francis Walsh, who died on August 20, 1940, was born in 1882. He attended the Boston Latin School, where he first acquired his appreciation of literature and the classics, which later became so integral a part of his life. Following his graduation from Harvard College he began the study of medicine, receiving his degree from the Harvard Medical School in 1908. After affiliation with various Boston hospitals, he was appointed to the Medical Staff of the Boston City Hospital in 1916. Because of his studious nature and painstaking attention to exact detail, he became interested in immunology and was physician-in-chief of the Department of Immunology when he died.

Such is the framework of his life, but to these meager details much could be added by the few intimates who knew and respected him. A recluse, he, like many retiring, quiet men, led a full life among his books and in his enjoyment of the fine arts. Always kind and courteous, he will be sadly missed by his many friends, he had no enemies.

CARMEL R. ALDEN, *Secretary,*
Senior Staff,
Boston City Hospital

DEATHS

CODMAN—ERNEST A. CODMAN, M.D., of Ponkapog, died November 23. He was in his seventy-second year. Born in Boston, he attended St. Mark's School and Harvard College and received his degree from the Harvard Medical School in 1895. Since graduation he had practiced in Boston. He was on the staff of the Harvard Medical School from 1900 to 1915, during which time he held the positions of assistant in anatomy, assistant in clinical and operative surgery, assistant in surgery and lecturer in surgery.

Dr. Codman was a fellow of the Massachusetts Medical Society, the American Medical Association and the American College of Surgeons, which he was instrumental in founding. He also held memberships in the American Surgical Association, the American Association for the Surgery of Trauma, the Society of Clinical Surgery and the New England Surgical Society. Last January he was one of three Boston doctors to receive the gold medal of the American Academy of Orthopaedic Surgeons for his work in building a system for the exchange of specific information on cases of bone sarcoma. He was a consulting surgeon at the Massachusetts General Hospital. His widow survives him.

HITCHCOCK—HENRY R. HITCHCOCK, M.D., of Plymouth, died November 23. He was in his eightieth year. Dr. Hitchcock received his degree from Harvard Medical School in 1890 and had practiced in Hyde Park before going to Plymouth in 1909. He was named physician of the United States Coast Guard in Plymouth and later served on the United States Public Health Service there.

Dr. Hitchcock was former assistant medical examiner for Suffolk County.

A member of the Massachusetts Medical Society and the American Medical Association, he was also a member of the Massachusetts Medico-Legal Society.

His widow and a son survive him.

MURPHY—THOMAS W. MURPHY, M.D., of Lawrence, died recently. He was in his seventy-first year.

Dr. Murphy received his degree from Tufts College Medical School in 1904 and was a retired member of the Massachusetts Medical Society and the American Medical Association.

MISCELLANY

BOSTON MEDICAL LIBRARY

VITTORIO PUTTI*
1850-1940

Putti, after thorough medical training, became the assistant to Vito Codivilla, director and chief surgeon of the Istituto Ortopedico Rizzoli in Bologna. Codivilla was one of the greatest orthopaedic surgeons of all time. He was the first to employ an aseptic method for skeletal traction in fractures and osteoperiosteal grafts of bone to encourage osteogenesis. It was he who first devised efficient methods for tendon transplantation and for gentle reduction of congenital dislocations of the hip. Putti worked under this master, and at his death succeeded him as the director of the institute, he was also made professor of orthopaedic surgery at the University of Bologna. He was an outstanding successor. Erudite, resourceful, skilful, with extraordinary executive ability, he built up the clinic to such an extent that it has become probably the most noted bone and joint center in the world. Some years ago the Clinical Surgical Club, whose members included the most famous American surgeons, made a series of visits to all the important surgical clinics of Europe. One of the members of the club after his return to America, said that in his estimation Professor Putti's clinic surpassed all the other clinics they saw, in organization, technique and efficiency. Putti was also chief surgeon to the Hospital for Tuberculosis at Cortina in the Dolomites and probably was responsible for its establishment.

Putti had close friends, in both England and America. He had great affection for Sir Robert Jones, and before World War II was in close touch with many other English orthopaedic surgeons, especially Professor Harry Platt, of Manchester. He visited this country in 1921, as guest of the American Orthopaedic Association, and for many years after that he was a frequent visitor. He delivered the Lane Lectures in California, and in 1931 was honorary chief surgeon of the Peter Bent Brigham Hospital, at Professor Harvey Cushing's invitation. In 1936 he was president of the Bologna congress of the *Societe internationale de Chirurgie orthopedique et Traumatologie*.

Putti contributed much to the advancement of bone and joint surgery, devising new nontraumatic methods for the early reduction of congenital dislocations of the hip, and being one of the first to report new methods and successful end results after arthroplastic operations. He originated and perfected various prosthetic apparatus in the extensive appliance shop that he established at the Istituto Rizzoli. His contributions to the literature of bone and joint surgery were valuable and many. His latest volume, *Cura operatoria delle fratture del collo del femore* was published in Bologna in 1940.

*Books and papers and other material by and about Dr. V. Putti are on exhibit in the funds of the Boston Medical Library.

About two years ago he suffered a severe attack of jaundice, from which he made a slow convalescence, but it had been believed in America that he had made a complete recovery. The exact cause of his death is unknown, but his passing has left a gap in the ranks of Italian, and indeed international, orthopedic surgeons that for the time being can hardly be filled. His legion of friends feel a sense of personal loss. His charm, his loyalty, his wisdom and his skill made him a unique character, commanding respect and compelling affection.

In addition to Putti's eminence in the field of orthopedic surgery, he gained for himself wide recognition as a medical historian. Brought up in an atmosphere of books, Putti found his greatest recreation in the history of his profession. The library in which he worked in Bologna, situated in a Benedictine monastery, known as *San Michele in Bosco*, was begun in the sixteenth century and contains manuscripts and books covering a period of over four hundred years. Not a prolific writer, he nevertheless made a distinct contribution to biography in a book entitled *Berengario da Carpi*, published in Bologna in 1937. This large quarto, handsomely printed and lavishly illustrated, contains the best account ever written of Berengario, the surgeon and pre-Vesalian anatomist who first drew anatomical figures from nature and depicted the separate muscles. Berengario taught surgery in Bologna from 1502 to 1527. In the biographical section of the book, Putti drew attention to many previously unknown editions of Berengario's works, particularly *De Fractura Caanii* (1518), which he translated into Italian as an appendix. The whole work is scholarly and could result only from profound and extensive research. Whatever claim to fame Putti may have found in his vocation, certainly his name will long be remembered for *Berengario*. He also wrote an article entitled "Historic Artificial Limbs," first published in the *American Journal of Surgery* (6:111-118 and 246-253, 1929) and later issued in book form (New York, 1930).

Putti was a handsome, vivacious, almost debonair person, a striking figure, both in Bologna on his orthopedic wards and in his medieval library. Both backgrounds were fitting, but we prefer to remember him in Cortina d'Ampezzo, high up in the Dolomites, one September day in 1932. Cushing, Klebs, Fulton and one of us were motoring through Italy after the Physiological Congress in Rome. We came to Cortina from Venice, crossing the Piave and going through the Fadalto Pass to Pieve di Cadore, where Titian was born. In glorious weather, the Dolomites stood out in bold relief as we entered the cup-shaped valley of Cortina. Here Putti met us, smiling, gracious and hospitable. He was justly proud of his hospital in Cortina, a "country branch" of the *Istituto Ortopedico Rizzoli* in Bologna. Facing south, in a warm valley, surrounded by green grass, with sheep nibbling in place of lawn mowers, this clean attractive hospital for patients with tuberculosis of bones and joints was obviously Putti's special pride. And well it might be, for the mahogany-brown patients, so hardened to exposure both summer and winter, that they lived out of doors practically unclothed the year around, were a living example of his skillful treatment. At a dinner that night, Putti was at his best as a genial host, but occasionally a faraway look came into his eyes, and a slight suggestion of sadness clouded his brow. Was the period of international exchange of companionship drawing to a close? Putti showed some uneasiness that night, as if his brilliant spirit were being dimmed. Parting the next day, one wondered what the future held for any of us, for we were certainly entering a new world and Putti, as well as the rest of us, was living in the past.

Unconsciously perhaps, Philippi Scaglietti, his first assistant physician in Bologna, paid to Putti the most fitting tribute, when he cabled one of us on November 1, 1940: "We are grieved to communicate the sudden death of our beloved master, Professor Putti." Master of orthopedic surgery, master of biography and bibliographic precision, Putti stands out as a towering figure, clean and straight as the Dolomites he loved so well.

H. R. V. and R. B. O.

NOTICES

ANNOUNCEMENT

HENRY R. VIETS, M.D., announces the removal of his office from 6 Commonwealth Avenue to 66 Commonwealth Avenue, Boston. Telephone KENmore 9430.

BOSTON DOCTORS' SYMPHONY ORCHESTRA



The Boston Doctors' Symphony Orchestra will rehearse under Alexander Thiede, formerly concertmaster of the Cleveland Symphony Orchestra, every Thursday at 8:30 p.m. Those interested in becoming members should com-

municate with Dr. Julius Loman, Pelham Hall Hotel, Brookline (BEA 2430).

HARVARD MEDICAL SOCIETY

The next meeting of the Harvard Medical Society will take place on Tuesday, December 10, in the amphitheater of the Peter Bent Brigham Hospital at 8:15 p.m.

PROGRAM

Presentation of cases.

The Relation of Forensic Medicine to Public Health.
Dr. Thomas A. Gonzales, chief medical examiner,
New York City.

NEW ENGLAND HEART ASSOCIATION

There will be a meeting of the New England Heart Association in the Moseley Building, Massachusetts General Hospital, on Monday, December 16, at 8:15 p.m.

PROGRAM

Resolution in honor of Dr. Henry Jackson, the first president of the New England Heart Association.

Mitral Stenosis after Eighty, with Especial Reference to Dr. Herman F. Vickery. Drs. Paul D. White and Edward F. Bland.

Arteriosclerotic Thoracic Aortic Aneurysms. Dr. M. deG. Ruffin. Discussion by Dr. Benjamin Castleman.

Right-Upper-Quadrant Abdominal Pain on Effort in Mitral Stenosis. Dr. Norman Boyer.

Comments on Lead 3 of the Electrocardiogram. Dr. Howard B. Sprague.

Further Experiences in the Newer Drug Therapy of Subacute Bacterial Endocarditis. Dr. C. Edward Leach. Discussion by Drs. James M. Faulkner, Charles N. Duncan, Sylvester McGinn and Saul R. Kelson.

Interested physicians and medical students are cordially invited to attend.

BOSTON MEDICAL HISTORY CLUB

There will be a meeting of the Boston Medical History Club at the Boston Medical Library, 8 Fenway, Boston, on Wednesday, December 11, at 8 15 p.m. Dr. Leonard Carmichael will speak on "Sir Charles Bell: His relation to problems of the present day."

All interested persons are cordially invited to attend.

WILLIAM HARVEY SOCIETY

The William Harvey Society of Tufts College Medical School announces the third lecture in its winter series, "The Functions of the Massachusetts Department of Mental Health, and the Preventive Program in Mental Hygiene," to be given by Dr. Clifton T. Perkins, commissioner of the Massachusetts Department of Mental Health. Dr. William Mahmud, clinical professor of psychiatry at Tufts, will preside at the meeting, which will be held on Friday, December 13, at 8 00 p.m., in the auditorium of the Beth Israel Hospital. Interested members of the medical profession are cordially invited.

ARLINGTON AND BELMONT MEDICAL CLUBS

A combined meeting of the Arlington Doctors' Club and the Belmont Medical Club will be held at Ring Sanatorium and Hospital, on Tuesday, December 10, at 8 00 p.m. Dr. Chester S. Keefer will speak on "The Sulfonamide Drugs in the Treatment of Infections." A social hour will follow the program.

APPOINTMENTS IN MEDICAL CORPS, REGULAR ARMY

An examination of applicants for appointment as first lieutenants, Medical Corps, United States Army, will be held within the continental limits of the United States from March 10 to 13, 1941, inclusive. Applications and requests for information concerning this examination should be addressed to the Adjutant General, War Department, Washington, D. C. Applications received after February 20, 1941, will not be considered.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING SUNDAY, DECEMBER 8

- MONDAY DECEMBER 9**
12 15-1 15 p.m. Clinicopathological conference Peter Bent Brigham Hospital Amphitheater
- TUESDAY DECEMBER 10**
9-10 a.m. Some Geographical Differences in Surgical Diseases Dr. Rudolf Nissen Joseph H. Pratt Diagnostic Hospital
12 15-1 15 p.m. Clinicopathological conference Peter Bent Brigham Hospital Amphitheater
8 p.m. Fractional Spinal Anesthesia Dr. M. J. Nicholson New England Society of Anesthesiology Massachusetts General Hospital
8 15 p.m. Harvard Medical Society Amphitheater Peter Bent Brigham Hospital
- WEDNESDAY DECEMBER 11**
9-10 a.m. Hospital case presentation Dr. S. J. Thannhauser Joseph H. Pratt Diagnostic Hospital
12 m. Clinicopathological conference Children's Hospital
8 15 p.m. Sir Charles Bell: His relation to problems of the present day Dr. Leonard Carmichael Boston Medical History Club Boston Medical Library 8 Fenway
- THURSDAY DECEMBER 12**
9 30 a.m. Combined clinic of the medical surgical orthopedic and podiatric services of the Children's Hospital and the Peter Bent Brigham Hospital at the Children's Hospital
9 10 a.m. Pathogenesis of the So Called Metatarsitis (General Paresis Tabes) Dr. Alfred Hauptmann Joseph H. Pratt Diagnostic Hospital

*8 15 p.m. Intraspinal Causes of Sciatica Dr. William J. Mixer
United States Marine Hospital, Chelsea

FRIDAY, DECEMBER 13

*9-10 a.m. Clinicopathological conference Dr. William B. Castle
Joseph H. Pratt Diagnostic Hospital
*8 p.m. Functions of the Massachusetts Department of Mental Health and the Preventive Program in Mental Hygiene Dr. Clifton T. Perkins William Harvey Society Auditorium Beth Israel Hospital

SATURDAY DECEMBER 14

*9-10 a.m. Hospital case presentation Dr. S. J. Thannhauser Joseph H. Pratt Diagnostic Hospital

*Open to the medical profession

DECEMBER 8-11—American Academy of Dermatology and Syphilology Page 831 issue of November 14

DECEMBER 10—Arlington and Belmont Medical Clubs Notice above

DECEMBER 10—International College of Surgeons Page 914 issue of November 28

DECEMBER 12—Pentucket Association of Physicians Page 263 issue of August 15

DECEMBER 16—New England Heart Association Page 956

DECEMBER 27-29—National Convention of the Association of Medical Students Boston

JANUARY 4, 1941—American Board of Obstetrics and Gynecology Page 787 issue of November 7

MARCH 8—American Board of Ophthalmology Page 201, issue of August 1

APRIL 21-25—American College of Physicians Page 1065 issue of June 20

MAY 21, 22—Massachusetts Medical Society Boston

JUNE 2-6—American Medical Association Cleveland Ohio

DISTRICT MEDICAL SOCIETIES

ESSEX SOUTH

JANUARY 8—Visceral Pain and Its Relief Dr. James C. White Danvers State Hospital Hathorne

FEBRUARY 5—Subject to be announced Lynn Hospital
MARCH 5—X-ray in Heart Disease Dr. Merrill C. Sosman Essex Sanatorium Middleton

APRIL 2—Pediatric Problems in General Practice Dr. Joseph Garland Addison Gilbert Hospital Gloucester

MAY 14—Relation of the Doctor to the Law Mr. Leland Powers New Ocean House Swampscott

FRANKLIN

JANUARY 14

MARCH 11

MAY 13

Meetings will be held at 11 a.m. at the Franklin County Hospital Greenfield

NORFOLK

JANUARY 28—Carney Hospital

FEBRUARY 25—Medico-Legal meeting 8 30 p.m. Hotel Puritan Boston

MARCH 25—To be announced

MAY 8—Censors meeting Hotel Puritan

SUFFOLK

JANUARY 29—Page 604 issue of October 10

APRIL 30—Page 604 issue of October 10

WORCESTER

DECEMBER 11—St. Vincent Hospital Worcester

JANUARY 8, 1941—Worcester City Hospital Worcester

FEBRUARY 12—Worcester State Hospital Worcester

MARCH 12—Memorial Hospital Worcester

APRIL 9—Hahnemann Hospital Worcester

Supper at 6 30 p.m. followed by a business meeting and scientific program

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in

regard to all listed books will be gladly furnished on request.

Clinical Urology. By Oswald Swinney Lowsley, A.B., M.D., director of the Department of Urology (James Buchanan Brady Foundation), New York Hospital, and Thomas Joseph Kirwin, M.A., M.S., M.D., attending surgeon, Department of Urology (James Buchanan Brady Foundation), New York Hospital. 8°, cloth; Vol. 1, 898 pp., with 220 illustrations; Vol. 2, 785 pp., with 145 illustrations, 7 plates and 9 tables. Baltimore: Williams & Wilkins Company, 1940. \$10.00 for the set.

Rose and Carless Manual of Surgery. American (sixteenth) edition. Edited by William T. Coughlin, B.S., M.D., professor of surgery and director of the Department of Surgery, St. Louis University School of Medicine; surgeon-in-chief, St. Mary's group of hospitals, St. Louis, Missouri. From the sixteenth English edition by Cecil P. G. Wakeley, D.Sc., F.R.C.S., F.R.S.E., F.R.S.A., F.R.A.C.S., fellow of King's College, London, senior surgeon, King's College Hospital; director of surgical studies and lecturer in surgery, King's College Hospital Medical School; surgeon, Belgrave Hospital for Children, and West End Hospital for Nervous Diseases; consulting surgeon, Maudsley Hospital and to the Royal Navy; Hunterian Professor, Royal College of Surgeons of England, and John B. Hunter, M.C., M.Chir. (Cantab.). F.R.C.S. (Eng.), surgeon, King's College Hospital; lecturer in surgery, King's College Hospital Medical School; surgeon, Royal Chest Hospital; consulting general surgeon, Throat, Nose and Ear Hospital, Golden Square. 8°, cloth, 1656 pp., with 1034 illustrations and 30 colored plates. Baltimore: Williams & Wilkins Company, 1940. \$9.00.

A Manual of Embryology: The development of the human body. By J. Ernest Frazer, D.Sc. (Lond.), F.R.C.S. (Eng.), professor of anatomy in the University of London. Second edition. 8°, cloth, 523 pp., with 282 illustrations. Baltimore: Williams & Wilkins Company, 1940. \$9.00.

Surgery of the Hand. By R. M. Handfield-Jones, M.C., M.S., F.R.C.S., surgeon to outpatients, St. Mary's Hospital; senior surgeon, Florence Nightingale Hospital; consulting general surgeon, Hospital for Women, Soho Square; consulting surgeon to the London County Council; lecturer in operative surgery, St. Mary's Hospital Medical School; late Hunterian Professor, R.C.S. 8°, cloth, 140 pp., with 95 illustrations. Baltimore: Williams & Wilkins Company, 1940. \$4.50.

The Control of Tuberculosis in the United States. By Philip P. Jacobs, Ph.D., director of personnel training and publications, National Tuberculosis Association. Revised edition. 8°, cloth, 387 pp. New York: National Tuberculosis Association, 1940. \$2.00.

History of Pharmacy: A guide and a survey. By Edward Kremers, Ph.G., Ph.M., Ph.D., Sc.D., former professor of pharmaceutical chemistry, University of Wisconsin, and George Urdang, Ph.G., D.Sc.Nat. 8°, cloth, 466 pp., with 30 illustrations. Philadelphia: J. B. Lippincott Company, 1940. \$4.50.

BOOK REVIEWS

The Diagnosis and Treatment of Cardiovascular Disease. Edited by William D. Stroud, B.S., M.D. Volume I, 4°, cloth, 832 pp., with 163 illustrations. Volume II, 4°, cloth,

855 pp., with 153 illustrations. Philadelphia: F. A. Davis Company, 1940. \$18.00.

These two large volumes, handsomely bound and copiously illustrated, consist of sixty-two chapters that range from the classification of cardiovascular diseases through congenital, rheumatic and other types of heart disease to electrocardiography, roentgenology, dysfunction, medical and surgical treatment, public-health problems and vascular anomalies. The work is an amplification of the section, "The Diagnosis and Treatment of Cardiovascular Disease," also edited by Dr. Stroud, and included in the *Encyclopedia of Medicine*, first published by the F. A. Davis Company in 1934.

The fifty-six contributors include many specialists in the field throughout the country. As is true of any such encyclopedic work, the quality of both the subject matter and the prose style varies considerably. However, the great bulk of the work is reliable and up to date, and these volumes, although not intended for the library of the general practitioner, should be useful as reference works in medical libraries, hospitals, medical schools and medical centers.

American Doctors of Destiny: A collection of historical narratives of the lives of great American physicians and surgeons whose service to the nation and the world has transcended the scope of their profession. By Frank J. Jirka, M.D., with an introduction by Harold W. Camp. 8°, cloth, 361 pp., with 20 portraits by Raymond Warren. Chicago: Normandie House, 1940. \$3.75.

Dr. Jirka has written an interesting, if somewhat unusual, history of American medicine. The book is built around his "doctors of destiny," one chapter being devoted to each character. The list sets the general tone of the book. With Shippen, Warren, Rush, McDowell, Drake, Morton, Holmes, Reed, Gorgas and possibly Weir Mitchell, Leonard Wood and W. W. Mayo as the chief candidates, most historians would agree. One misses Waterhouse, Hosack, Physick and a number of others. Jirka adds Henry Dearborn, Samuel A. Mudd, Charles Norris, Franklin H. Martin, Leo L. Stanley, James S. Greene and Frederick Tice, some of whom are almost unknown and are of such slight importance that their inclusion is hardly justifiable. His loyal Chicago associations have served to unbalance an otherwise well-conceived book. There is a final chapter, with a portrait, on the work of Frank J. Jirka, the author. The book is only slightly documented, and some statements are open to question. There are many other books covering the same ground that are far superior to Dr. Jirka's efforts as a medical historian. A series of twenty portraits, painted for this book, do not add to its value.

Manual of Dermatology. By Carroll S. Wright, B.S., M.D. 8°, cloth, 376 pp., with 138 illustrations. Philadelphia: Blakiston Company, 1940. \$4.00.

This manual was written chiefly for medical students and general practitioners. It is useful as a ready reference book since the average textbook in dermatology is too voluminous to be practical. The method of presentation corresponds with the previously published compend, *Diseases of the Skin*, by Jay F. Schamberg, with some reclassification of the text and many new photographs added. The volume can be recommended as a practical, compact volume to be amplified by the larger textbooks for those who wish more complete subject matter and bibliography.

The New England Journal of Medicine

Copyright, 1940, by the Massachusetts Medical Society

VOLUME 223

DECEMBER 12, 1940

NUMBER 24

RELATION OF PYELONEPHRITIS AND OTHER URINARY-TRACT INFECTIONS TO ARTERIAL HYPERTENSION*

SOMA WEISS, M.D.,† AND FREDERIC PARKER, JR., M.D.‡

BOSTON

ALTHOUGH as early as 1882 Wagner¹ described cases corresponding to pyelonephritis, and Göppert² in 1908 called attention to the frequency and occasional chronicity of "pyelitis," it is only in recent years that the natural history and clinical significance of pyelonephritis have been fully recognized. In America attention was called to certain aspects of this disease chiefly by Longcope,³ Peters⁴ and their associates. There are several reasons for this relatively slow recognition of the clinical characteristics of pyelonephritis. This disease has a strikingly variable clinical course and structural lesions. In the majority of cases the acute renal infection is benign and heals spontaneously, leaving behind only small renal scars. In others, however, the infection is chronic or recurrent, and the inflammatory tissue reaction gradually involves the entire kidney, unilaterally or bilaterally. Another characteristic of the disease, which has made the recognition of its natural history difficult, is the difference in the clinical features at various stages. Thus, whereas in the active infectious stage "pyuria" with symptoms of infection referable to the kidneys, ureter, bladder or urethra dominates the clinical picture, in the chronic, healed or healing stages symptoms of active infection and pyuria are often absent, and the clinical course is like that of chronic Bright's disease with arterial hypertension or renal failure.

During the last six years, we have studied a group of 100 patients suffering from pyelonephritis, with a detailed clinical and morphological investigation in various stages from the acute to the terminal chronic or healed. The results of

this study together with the literature on the subject can be found elsewhere.⁵ Since the publication of this report, additional selected cases have been studied. The purpose of this discussion is to summarize the present status of our knowledge in the light of personal experience.

STAGES OF PYELONEPHRITIS

We have classified pyelonephritis in four groups, according to the various stages of the disease: acute (pyelitis), chronic (active), healed and healed with recurrence. Acute pyelonephritis may heal, or may become chronic. Chronic pyelonephritis may persist or heal. Healed pyelonephritis may be followed by attacks of acute or chronic pyelonephritis. Each of these stages may occur either unilaterally or bilaterally.

This classification was made primarily on the basis of the combined clinical and histological evidence, but neither the specific causative organisms nor the mode of origin of the bacterial renal infection was taken into consideration. Such a relatively simple classification is justified because in most cases even the combined clinical, bacteriological and morphological evidence fails to reveal with any degree of certainty whether one is dealing with pyelonephritis of hematogenous (descending), urogenous (ascending) or lymphatic origin. We have not considered interstitial nephritis as pyelonephritis. Just as in other types of Bright's disease, without a detailed history including previous clinical studies, diagnosis of the various stages of pyelonephritis may be difficult.

The main morphologic characteristics of acute pyelonephritis consist in acute local or diffuse infection and inflammatory processes in the interstitial tissues, the tubules and the pelvis. In chronic and healed pyelonephritis, the main renal changes are as follows: inflammatory reaction with or without infection of the interstitial tissues; colloid casts

*From the Medical Clinic, Peter Bent Brigham Hospital, and the Mallory Institute of Pathology, Boston City Hospital.

Presented before the annual meeting of the Massachusetts Medical Society, Boston, May 21, 1940.

†Mercy Professor of the Theory and Practice of Physic, Harvard University, physician-in-chief, Peter Bent Brigham Hospital.

‡Associate professor of pathology, Harvard University, pathologist-in-chief, Boston City Hospital.

in the tubules, which are lined with atrophic epithelium; periglomerular fibrosis; evidence of infection or inflammation in the tubules; and frequently acute, subacute or chronic vascular lesions. The relative involvement of the interstitial tissues and tubules varies considerably from case to case. The clinical picture in the chronic stage is determined either by the vascular and the corresponding hypertensive elements, or by the disturbance of the excretory function of the kidney, depending on whether the interstitial tissues or the tubules are primarily affected.

Acute pyelonephritis. Acute pyelonephritis is the commonest disease of the kidneys. Its clinical features correspond to those recognized under the term, "pyelitis." In our experience the infection almost always involved the renal parenchyma as well as the pelvis, and hence "pyelitis" is a misnomer. The nature of the parenchymatous involvement is essentially the same, irrespective of the type or origin of the infection. Occasionally infection of the interstitial tissue without involvement of the nephron accounts for cases with all the systemic manifestations of the disease, including pain of renal origin, but without the characteristic urinary findings. Acute vascular lesions develop at times in the early stage of pyelonephritis, and it is of special interest that in some cases hyperplastic arteriolosclerosis developed within as short a time as six months after the onset of infection. Arterial hypertension, however, is usually absent in acute pyelonephritis. This observation is in harmony with previous conclusions that under certain circumstances severe obliterative arterial or arteriolar lesions may develop within as short a period as a month or two.

Chronic (active) pyelonephritis. In some persons renal infection with pyuria and bacteriuria may persist for months and years. The symptoms and other features referable to such chronic renal infection vary according to the severity and extensiveness of the infection and the degree of impairment of renal function. Arterial hypertension is frequently associated with this stage. Although the arterial hypertension is often severe (malignant) in contrast to other types of hypertension generalized atherosclerosis, cerebrovascular accidents, coronary disease and thrombosis are not prone to develop. Chronic pyelonephritis of childhood may be associated with general underdevelopment and changes in the bones. The cause of death, if it is related to the pyelonephritis, is usually uremia, vascular encephalopathy or heart failure.

Healed (diffuse) pyelonephritis. Healed (diffuse) pyelonephritis represents the healed or non-infectious stage of the acute or chronic (active) dis-

ease. Frequently the clinical diagnosis of this stage, particularly without a history of active infection in the past, is difficult or not feasible, because the clinical features closely resemble the terminal stage of benign or malignant nephrosclerosis (essential hypertension) or chronic glomerulonephritis. Since the majority of cases of acute pyelonephritis (pyelitis) heal, leaving behind small pyelonephritic scars, this type of healed focal pyelonephritis has no special clinical significance. This is also attested by the frequency of the "accidental" discovery of the scars during routine post-mortem examination. There are, on the other hand, an appreciable number of patients who, after suffering from chronic pyelonephritis or from repeated attacks of the acute form, apparently recover from the active infection but subsequently develop arterial hypertension, with or without renal failure. Clinical manifestations of active renal infection are lacking in these patients. There may be an increased number of white cells in the urine from time to time, but in many cases even repeated counts (Addis and Oliver⁶) fail to reveal abnormal elevations. If the hypertension is severe, showers of red blood cells may appear periodically in the urine. This phenomenon is due to ruptured capillaries or arterioles within the urinary passages. The pyelogram may show deformities of the pelvis, calyces and ureters. Children or young adults suffering from persistent pyelonephritis may remain underdeveloped and may at times have changes, with deformities, in the bones or in the function of the glands of internal secretion. Frequently the bony abnormalities grossly resemble those seen in rickets, and hence are often said to be due to "renal rickets." In our experience, however, they do not correspond to the bony changes of true rickets as indicated by roentgenographical and histological evidence. Often they manifest themselves in increased or decreased density of the bones, and at times areas exhibiting both types of changes may be present within the same bone (Case 1).

Histologically, healed pyelonephritis is characterized by lymphocytic infiltration of the interstitial tissue and the pelvis and by colloid casts in the tubules. Mallory, Crane and Edwards⁷ were able to reproduce this condition experimentally. Arterial hypertension is frequently associated with healed diffuse pyelonephritis, and it may develop long after the active infection, as indicated by clinical evidence, has healed. The inflammatory tissue reaction, precipitated by the infection, and hence the syndrome of hypertension, can advance long after the infection itself has subsided. The hypertension of healed pyelonephritis, which often dominates the clinical picture, is frequently severe and is manifested in headache, vertigo, vascular

crisis, pronounced changes in the eyegrounds and elevation of the spinal-fluid pressure, accompanied at times by increased protein content of the fluid. Elevation in the spinal-fluid pressure is prone to be associated with albuminuric retinitis, high diastolic pressure, cerebral encephalopathy and uremia. Cardiac asthma and other manifestations of left ventricular failure frequently occur. Atherosclerosis, coronary sclerosis and thrombosis, and cerebrovascular accidents, on the other hand, are seldom associated with this type of hypertension.

Healed pyelonephritis with recurrence. Patients with pyelonephritis are predisposed at times to recurrent attacks, due usually to anatomic abnormalities of the kidney or of the urinary passages, or

pneumonia and scarlet fever with otitis media. She was first observed in September, 1925, in another hospital, where the case was diagnosed as acute gastrointestinal intoxication and otitis media. In October, 1925, pyuria with a + test for albumin was first noted, and numerous white blood cells were found in the urine. Every urine specimen examined thereafter showed the presence of pus. A tonsillectomy and adenoidectomy were performed in 1932, at which time enuresis also was one of the symptoms. Since 1934, when the patient was 9, frequent and painful urination had been noted. In 1935 there were vomiting and intermittent abdominal pain.

Some of the clinical and laboratory findings from this date on are charted in Figures 1 and 2. The blood pressure at that time was 186/130. The kidney function was considerably reduced, the urea clearance being 19 per cent. The maximum specific gravity was 1.014. X-ray studies suggested a tumor of the right kidney, but surgical exploration failed to reveal one. A biopsy specimen of the right kidney five years before the patient's death revealed histologic changes characteristic of chronic pyelonephritis with thickening of the small arterioles. The sections showed numerous pyelonephritic scars. Some of the tubules contained colloid casts; others were atrophic. The arteries within the scars showed productive endarteritis, and the arterioles hyperplastic arteriosclerosis. There was considerable lymphocytic infiltration of the interstitial tissues. The glomeruli and the tubules in the nonscarred areas were essentially normal, whereas the blood vessels showed changes similar to but much less marked than those in the scarred areas. The pelvis was infiltrated with lymphocytes, plasma cells and occasional polymorphonuclear and eosinophilic leukocytes. In addition there were fairly numerous lymph follicles beneath the pelvic epithelium. The diagnosis of chronic pyelonephritis with pyuria, arterial hypertension and nephrosclerosis was made.

Following surgical recovery, the pyuria and the hypertension persisted, as indicated in Figure 1. The patient suffered from severe attacks of headache. Mandelic acid therapy failed to clear up the renal infection. In 1936 the aortic second sound became loud, and for the first time the heart was found to be enlarged. The patient showed only occasional and slight elevation of the temperature. Frequent analyses of the urine showed large numbers of white blood cells and on most occasions varying amounts of albumin. The specific gravity ranged between 1.017 and 1.020. A dilution-concentration test in August, 1936, showed a variation of only 1.001 and 1.012, and the urine culture showed a heavy growth of *Escherichia coli*. The blood hemoglobin was 12.5 gm. (74 per cent), and the red-cell count was 5,620,000. The white-cell count was 15,250, with normal smear and differential. In September, 1936, the carbon dioxide combining power was 40 vol. per cent, and the nonprotein nitrogen 60 mg. per 100 cc. The results of the other laboratory investigations, including serological tests, were normal and noncontributory.

During 1937 her general condition remained satisfactory, although the arterial pressure was high and for the first time definite evidence of retinal arteriosclerosis was noted. In November, 1937, the patient developed profuse menstruation. At that time x-ray films of the kidney and bladder region failed to show the kidney outlines. There was a considerable degree of pyuria. In December the eyegrounds showed marked arteriovenous nicking and very early spots of degeneration of the retina. In February, 1938, bilateral pyelograms revealed definite deformities of both renal pelvis, and the kidney outlines appeared to be quite small. The urine culture still showed *Esch.*

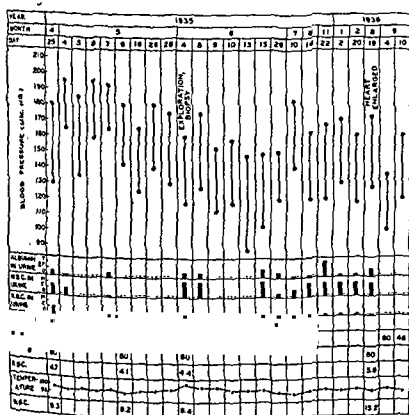


FIGURE 1. Case 1.

The clinical course of pyelonephritis.

to certain foci of infection. Such recurrences may develop after previous attacks of infection have healed. In these cases the clinical and histologic changes represent a combined picture of healed pyelonephritis and acute or chronic active pyelonephritis. The clinical diagnosis often depends on the availability of a history of past infections and of long infection-free periods.

The following two cases are reported as instructive examples of the natural history of pyelonephritis and the relation of urinary-tract infections to the development of arterial hypertension.

CASE 1. C. W. F. M., a 15-year-old schoolgirl, was admitted to the Peter Bent Brigham Hospital for the last time on January 26, 1940, with the complaint of fatigue, lethargy, anorexia and intermittent spasms of the limbs of 2 months' duration. The family history was irrelevant.

The present illness dated back to infancy, when between the ages of 6 months and 1 year the patient suffered from

coli. The urine was of low specific gravity, with a slight trace of albumin, and the sediment continued to contain white blood cells. The vital capacity of the lungs was 2000 cc. In March, 1938, an increase in the severity of headaches was noted.

In May, 1938, the patient was again examined in the Peter Bent Brigham Hospital. No exudate, scars or hemorrhages of the retinas were observed. The heart sounds were somewhat accentuated, and both the aortic and pulmonary second sounds were quite loud. The rest of the

with left ventricular hypertrophy. The lungs were clear. A kymogram showed regular and fairly active heart beats along the left border. The maximum systolic contraction was about 5 mm. Aortic pulsations were normal. The vital capacity of the lungs was 1450 cc. and later 1750 cc. Two electrocardiograms revealed prolonged QT interval (0.40 second) and an abnormal T wave in Lead 4.

X-ray films of the skull, spine, pelvis and long bones showed diffuse changes, with coarse mottling of some of the bones,—particularly in the cranial vault,—and with zones of increased density parallel to the vertebral plates, most marked in the lumbar vertebrae. There were no rachitic changes along the epiphyses, several of which were still visible. There were small concave areas of erosion in each humeral diaphysis close to the upper epiphysis.

On admission the hemoglobin was 40 per cent, the red-cell count 2,360,000. A smear indicated hypochromic anemia. The white-cell count was 6500. The blood Wassermann and Hinton tests were negative. The stool showed +++ guaiac and ++++ benzidine tests. The specific gravity of the urine varied between 1.012 and 1.014, with a trace of albumin and 2 to 12 white blood cells per high-power field. Finely, granular brown casts were present on several occasions. The urine cultures showed *Staphylococcus aureus* and *Aerobacter aerogenes*. The blood urea nitrogen gradually rose to 285 mg. per 100 cc. The total blood protein was 6.2 gm., the albumin 3.5 gm., and the globulin 2.7 gm. The blood calcium was 5.5 and 3.6 mg. per 100 cc. on two examinations; the phosphorus was 11.3 mg., and the chlorides 651 mg.

The patient lost 33 pounds in weight during the 21 days in the hospital. Soreness of the mouth and severe abdominal cramps developed. Later, soreness of the genitalia was the main complaint. She gradually lapsed into coma and died on February 15.

Autopsy. The pericardium contained 30 cc. of straw-colored fluid. The heart weighed 310 gm. The left ventricle was hypertrophied. The coronary arteries were normal. The kidneys were extremely small, the right weighing 25 and the left 30 gm., and were firm, reddish brown and finely granular, without retracting scars. The capsules stripped with difficulty. The cortices were only 1 mm. in thickness. The calyces were greatly dilated and extended up to 1 or 2 mm. from the capsular surface. The ureters were moderately dilated, measuring 7 mm. in diameter. Constrictions were not observed, and the walls were not thickened. No ureteropelvic or ureterovesical valves were noted. The adrenal cortex contained a few small adenomas. The bladder was normal in size, with slight injection of the trigone. The rest of the examination failed to reveal pertinent findings.

On histologic examination the right kidney showed a rather diffuse increase in connective tissue. The scars were of varying ages. In the older scars the few persisting tubules contained colloid casts. The vascular changes were similar to those described in the biopsy specimen, obtained 5 years previously. In the more recently scarred areas, many of the tubules contained pus and showed abscess formation. The vessels in these areas showed a moderate degree of change. The nonscarred areas showed dilated tubules. The glomeruli were decreased in number and showed hypertrophy and various stages of alternative glomerulitis. The vascular changes were moderate. The pelvis showed marked infiltration of the subepithelial tissue with lymphocytes and plasma cells. The left kidney showed essentially the same picture. The mucosal surface of the bladder was completely denuded of epithelium. Throughout the submucosa there was considerable increase

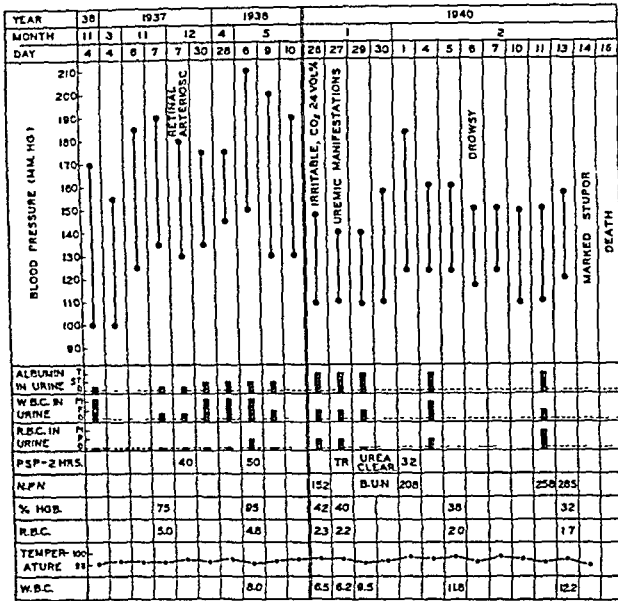


FIGURE 2. Case 1 (continued).
The later clinical course of pyelonephritis.

findings were irrelevant. In addition to the data presented in Figure 2, on two occasions the culture of the urine was sterile.

During 1939 the patient attended school regularly. In March, 1939, the school physician reported the blood pressure as 230/155 (not recorded in Fig. 2). In November the patient developed anorexia, became somewhat drowsy, and began to lose weight. She gradually developed increasing pallor and became irritable. Dyspnea appeared on exertion. In December, 1939, she developed cramping sensations in the fingers, hands, arms, feet and legs.

When admitted to the Peter Bent Brigham Hospital in January, 1940, the patient was thin and lethargic. Marked changes were present in the retinas of both eyes. There were numerous white patches over both fundi and an increase of physiologic cupping on the right. The arteries were tortuous and narrowed and showed increased light reflexes; no hemorrhages could be seen. The heart was enlarged. There was a presystolic gallop rhythm, and a blowing systolic murmur over the entire precordium. There were involuntary twitching movements of both arms and legs. Interference with venous return of the arms and legs precipitated carpopedal spasm. There was a generalized adenopathy in the cervical, axillary and inguinal regions. The rest of the examination was negative.

During her stay in the hospital the patient became increasingly apathetic. The breathing became deeper. On January 27 the carbon dioxide combining power was 24 vol. per cent, with the blood urea 158 mg. per 100 cc. A 7-foot film showed the heart to be above normal limits,

in hyalinized connective tissue and lymphocytic cell infiltration. The parathyroid glands were greatly enlarged and composed primarily of cords of columns of sheath cells. Most of these cells had a dense eosinophilic to amphiphilic type of cytoplasm. In a few areas the cells had a water clear cytoplasm, were slightly enlarged and showed slight eccentricity in the position of the nuclei.

CASE 2 H E B S, a 45 year old housewife, was admitted to the Peter Bent Brigham Hospital, April 22, 1940, with the chief complaints of headache for 6 weeks and nausea and vomiting for 2 days.

The illness dated back to January, 1921, when, during her first pregnancy, she developed acute pyelonephritis (pyelitis) with frequency of urination and bilateral lumbar pain, more acute on the left. On examination there

results of the physical examinations were essentially negative. Ascending pyelograms revealed that the pelvic portion of the left kidney was rounded and the calyces somewhat blunted. The right renal pelvis appeared to be larger and somewhat more irregular than the left. Cystoscopic examination failed to reveal evidence of cystitis. Cultures of the urine specimens obtained from each of the ureters yielded *Esch coli*. There were numerous white cells in each of the catheter specimens. The specific gravity of the urine was 1.025. On this occasion the diagnosis of chronic pyelitis was made for the first time.

The patient had contracted syphilis following discharge from the hospital, and a blood Wassermann test became positive. She received antisyphilitic treatment. In 1925 the pain in the left upper quadrant and the pyuria returned. During February, 1926, she had chills and fever on an average of once a week, and later the pain in the left loin became accentuated. In August 1926, there were tenderness and a questionable mass in the region of the left kidney. The blood pressure was still normal. At this time cystoscopy failed again to reveal evidence of cystitis. The orifice of the left ureter was slightly redened. The catheter passed easily to the right pelvis. The urine obtained on the right was clear, and the culture sterile. A pyelogram on the right indicated a slightly dilated pelvis and rounded calyces. The dye appeared at the end of the catheter in 5 minutes. The catheter introduced into the left ureter passed only a distance of 65 cm. The urine collected was cloudy, and the culture yielded *Esch coli*.

On September 1, 1926, a left nephrectomy was performed by Dr. William C. Ounby. The kidney was very small, measuring 7 by 5.5 cm., and was 3 cm. thick. The pelvis was dilated. Very little kidney substance was seen. A small quantity of puriform material could be squeezed out of the tissues. Histologic examination showed focal scars due to healed pyelonephritis, as evidenced by the presence of colloid casts, periglomerular fibrosis and interstitial infiltration with lymphocytes. In these scars the arteries showed a rather marked degree of proliferative endarteritis, and the arterioles hyperplastic arteriosclerosis. In the unaffected areas the renal tissue was essentially normal, and the blood vessels showed no changes of any significance. In the connective tissue beneath the pelvic epithelium were numerous lymphocytes and plasma cells and a moderate number of eosinophils and polymorphonuclear leukocytes. In addition there were lymph follicles with active germinal centers. The diagnoses were healed pyelonephritis, with some activity in the pelvis and probable congenital hypoplastic kidney.

Following nephrectomy the patient improved, although she re-entered the hospital in June, 1927, with symptoms suggestive of chronic endocervicitis. She was quite well from this time until January, 1930, when she developed sudden and severe pain in the right flank, followed by nocturia (eight or ten times). Examination showed marked tenderness in the right flank, the right kidney was palpable. Cystoscopic examination showed considerable reddening of the mucosa of the bladder. The right ureteral opening showed some edema about the orifice. The phenolphthalein output of the kidney was 60 per cent. During the hospital stay urine specimens from the right ureter were obtained on three occasions, and the culture of each yielded *Esch coli*. The urine contained a slight trace of albumin and many white cells. A blood Wassermann test was positive. The blood pressure was still normal. The diagnosis made was recurrent acute pyelitis. For 3 years thereafter, the patient had complete relief from renal and urinary symptoms but in 1933 she

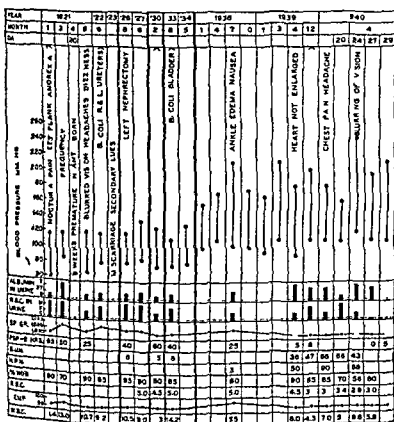


FIGURE 3 Case 2

The clinical course of pyelonephritis. The arrow heads below the day line indicate that the urine cultures were positive for *Escherichia coli*.

was a systolic murmur, but as shown in Figure 3 the arterial pressure was normal. Cystoscopic examination failed to reveal evidence of cystitis. A specimen of urine obtained from the left ureter was hazy, and urine cultures from both the left and the right ureter yielded *Esch coli*. The urine from the left ureter contained a large number of white blood cells. The phenolphthalein renal function test was 65 per cent. The temperature during this hospital stay was essentially normal. The patient was discharged improved.

After discharge the urinary symptoms became aggravated and the patient developed a low grade fever. She was followed in the Outdoor Department and received pelvic lavage of the kidneys in February and March, 1921. At this time the urine showed a large trace of albumin, and the sediment contained many white blood cells. Following the birth of a 5 weeks-premature baby the urinary frequency continued, but the urine contained only a few white cells. There was marked costovertebral tenderness over the left lumbar area, and a slight degree over the right. In 1922 the patient felt fairly well although she occasionally suffered from pain in the left flank. An increased number of white cells persisted in the urine. The

developed pain in the right upper quadrant radiating to the interscapular region. Icterus of the scleras had been observed at times. In August, 1933, physical examination was essentially normal. The cholecystogram revealed a normal gall bladder. Cystoscopic examination and the urine sediment obtained from the right ureter were normal, but culture of the urine yielded *Esch. coli*. The other laboratory findings were essentially unchanged.

In 1938 the patient again entered the hospital, complaining of pain in the right flank, chills and fever. For the first time she suffered from dizzy spells and swelling of the ankles. The physical examination was essentially normal. The blood pressure was elevated. On cystoscopic examination the bladder was normal. An intravenous urogram failed to show any definite excretion. The urine specimen obtained from the right ureter was sterile. The patient improved and was discharged from the hospital. In 1939 she developed pain in the left breast, and also began to experience attacks of dizziness and weakness. On examination the eyegrounds were normal except for slight arteriovenous nicking. The heart was normal. The palpable arteries were not thickened. The rest of the examination was negative. The blood pressure was elevated (Fig. 3). The vital capacity of the lungs was 2100 cc. A 7-foot film of the heart indicated that the size was just within normal limits. The electrocardiogram was normal except for left-axis deviation. Renal tests indicated lowered function. It is of interest that the white-cell count in the urine was not elevated on repeated examination. The discharge diagnosis in May, 1939, was pyelonephritis with arterial hypertension. On numerous occasions after discharge the patient experienced thoracic pain, with radiation down the left arm; this was brought on by slight exertion and by emotional distress. In addition the pain in the right flank, accompanied by nocturia and pyuria, became severe. Repeated examination of the urine in the Outdoor Department revealed persistent albuminuria and pyuria. In December, 1939, the patient developed constant nausea and frequent attacks of vomiting associated with headache and dizziness. Examination revealed slight arteriovenous nicking of the vessels of the eyegrounds and moderate enlargement of the heart. A split second sound was present with a systolic murmur. Exquisite tenderness was present over the right flank posteriorly. Other data obtained are presented in Figure 3. The urine showed increased white cells, and the culture yielded *Esch. coli*. X-ray films failed to reveal the outline of the right kidney or the presence of stones. The electrocardiogram remained as before. The patient was discharged in January, 1940, in an improved state.

In March, 1940, the severe throbbing headache returned, and in April the pain in the right flank again became severer. The patient was nauseated, and vomited on several occasions. She also experienced palpitation and sensations of constriction in the substernal region, accompanied by increasing weakness. The results of the examination during hospitalization were essentially unchanged, with a few exceptions. The systolic murmur was more pronounced. The arterial pressure was higher. For the first time several fresh linear hemorrhages and an increase in the light reflex of the arteries of the eyegrounds were observed. The arteries were narrow and varied in caliber. The dynamics and chemical constituents of the spinal fluid were normal. Urine cultures revealed *Staph. aureus* in small numbers, and in one specimen nonhemolytic enterococci. Other pertinent data are presented in Figure 3. After discharge from the hospital, the patient was last seen in July, 1940, when the symptoms were mainly cardiac and hypertensive in origin.

These two cases are instructive in demonstrating the clinical course of the severe form of pyelonephritis. In Case 1 the renal infection started at the age of six months, and persisted until the death of the patient at fifteen years. Whereas local symptoms with pyuria dominated the clinical picture in early childhood, Bright's disease with arterial hypertension was the presenting syndrome during the last two years. The cause of death was uremia, and at the time of death the renal infection still persisted. Hence the case represents chronic (active) pyelonephritis. The kidneys at post-mortem examination were unusually small, but without congenital abnormalities. In our opinion this type of kidney is caused by lack of normal growth due to chronic infection, rather than by contraction of the kidney.

Case 2 represents the late effects of pyelonephritis in adult life. In this patient the first attack developed during pregnancy. The left kidney, removed surgically, was small and probably congenitally hypoplastic. Whether the right kidney has any congenital malformation cannot be stated with certainty. During the twenty years that this patient has been studied, she has suffered from repeated attacks of acute infection, suggesting healed and recurrent pyelonephritis. The gradual onset of hypertension is clearly demonstrated in this case. For the first seventeen years, symptoms referable to the urinary system and pyuria were the main features, and the blood pressure was normal. Symptoms of severe hypertension, with changes in the eyegrounds, and angina pectoris developed during the last three years.

VASCULAR CHANGES AND THE ARTERIAL HYPERTENSION OF PYELONEPHRITIS

In acute pyelonephritis the inflammatory tissue reaction may at times involve the renal arterioles and venules. In the cases we observed, such lesions usually consisted of a deposition of fibrin in the wall of an arteriole and of infiltration of polymorphonuclear leukocytes and mononuclear cells. At times partial or complete thrombosis of the vascular lumen or proliferation of the endothelium developed.

In chronic or healed pyelonephritis, vascular lesions in the kidneys are often prominent, involving both the interarcuate renal arteries and the arterioles. In the arteries there is increased connective tissue in the intima. The internal elastic membrane is frequently duplicated. The walls of the arterioles are thickened as a result of concentric proliferation of the cells (hyperplastic arteriosclerosis). Hyalinization of the arterioles develops only rarely. Arteriolar necrosis and acute

arteriolitis resembling periarteritis nodosa also occur in some cases. It is of interest that in cases of cystitis, hydronephrosis and renal tuberculosis, uncomplicated by pyelonephritis, vascular changes and hypertension did not occur. These morbid states, as well as infections of the urethra or of the bladder, are not responsible, as a rule, for hypertension. The presence of deformities of the renal pelvis and of the ureters in patients with arterial hypertension does not justify, *per se*, the conclusion that it bears a causative relation to the renal origin of hypertension. In many cases the changes in the urinary passages are but incidental findings in persons with "primary" nephrosclerosis. This has not been taken into consideration by some investigators. A relation was found between arterial hypertension and the severity and diffuseness of the obliterative vascular lesions caused by pyelonephritis. On the other hand, a close correlation between arterial hypertension and the size or the functional capacity of the kidneys was not noted. Thus the kidney in chronic or healed pyelonephritis may be normal in size, and yet insufficient because of the obstructed tubules.

Our studies indicate that the vascular changes in pyelonephritis are proliferative rather than degenerative. Because in focal pyelonephritis the vascular changes are usually localized within areas corresponding to the inflammatory tissue reactions, and because in unilateral pyelonephritis, without long persisting arterial hypertension, the vascular changes are present only in the affected kidney, we concluded that the vascular changes are caused primarily by the inflammatory tissue reactions of pyelonephritis and not by hypertension. This concept is supported also by the fact that a moderate degree of diffuse arteriolar change is present without, and presumably before, the development of hypertension. However, because in unilateral pyelonephritis with severe hypertension some arteriolar lesions subsequently develop in the unaffected kidney, hypertension is thought to be an accelerating or intensifying factor. Thus in the development of vascular changes we are dealing with a vicious circle precipitated by pyelonephritis and, in turn, accentuated and accelerated by hypertension. The specific factors suspected of being responsible for the vascular lesions observed in pyelonephritis are slow blood flow, intravascular pressure and local edema of the vessels. Thus the mechanism of the development and the morphologic characteristics of these renal vascular lesions are not unlike those of the lesions in the lungs in certain cases of mitral stenosis.⁸ Similar types of vascular lesions were also observed in a variety

of conditions, as either a systemic or a localized vascular response to certain noxious stimuli. They may be present in carcinomatous lymphangitis or in emphysema of the lungs, and around gastric and duodenal ulcers, indicating that not infection but inflammation is the essential factor for the development of these proliferative vascular lesions. Because the vascular lesions in pyelonephritis are highly proliferative and are similar to those found in the usual type of malignant nephrosclerosis, there is a great tendency in chronic or healed pyelonephritis to severe renal ischemia and hence to severe hypertension. It has been estimated that pyelonephritis is responsible for 15 to 20 per cent of all cases of malignant hypertension.

Of 20 autopsied cases with unilateral chronic or healed pyelonephritis the blood pressure had been normal in only 8. The size of the affected kidney was usually greatly diminished, whereas the unaffected kidney was often enlarged. The vascular changes in the affected kidney in cases with normal blood pressure varied from moderate to severe, with the unaffected kidney showing no appreciable changes. In cases of hypertension the affected kidney showed marked vascular changes, and the unaffected side showed slight to moderate changes.

In one group of patients with chronic or healed pyelonephritis the kidneys were unusually small. In our experience the smallest kidneys in cases of chronic Bright's disease were those caused by pyelonephritis. In several of these, no abnormalities of the pelvis, ureter, bladder or urethra were found. The blood pressure in most cases was very high, but in others only slightly elevated. The evidence we gathered indicates that renal infection beginning in early childhood with resultant scarring that interferes with normal renal growth can account for the markedly reduced size of the kidney. It is probable, however, that congenital hypoplastic or so-called "hypogenetic" kidneys, particularly if they are associated with congenital malformation of the urinary passages, predispose to chronic pyelonephritis, and a combination of such congenital renal malformation with pyelonephritis is responsible in some cases for such unusually small kidneys. Some clinicopathological correlation suggests that congenital hypoplastic or hypogenetic kidneys even without complicating pyelonephritis may eventually lead to uremia. Obviously these small kidneys are not "primary" or "secondarily contracted," but are the result of a lack of physiologic growth. The rapidly increasing discrepancy between the size and function of the body and that of the kidneys leads finally to uremia, usually in early adult life.

PYELONEPHRITIS AND TOXEMIA OF PREGNANCY

The interrelation between pyelonephritis and toxemia of pregnancy deserves special consideration. In our experience acute pyelonephritis (pyelitis) per se is usually not responsible for toxemia of pregnancy. It is of interest, on the other hand, that in a group of 8 women with arterial hypertension and with small chronic or healed pyelonephritic kidneys post mortem, 6 had had attacks of toxemia. In a recent study of toxemia of pregnancy ("the vascular syndrome of pregnancy") we⁹ concluded that, although the average incidence of toxemia of pregnancy was 3 per cent in all cases of pregnancy, in patients with pre-existing arterial hypertension, not considering the specific etiology, it was 50 per cent. It is probable that in a group of patients with chronic or healed pyelonephritis associated with hypertension and with low-reserve kidneys, the incidence of toxemia will be found even higher. In spite of this high incidence, in the *total group* of toxemias pyelonephritis plays a relatively small role. Thus in a group of 60 cases studied clinically only 3 patients had chronic pyelonephritis associated with prepregnant hypertension. Similarly in a group of 26 autopsied cases with fatal eclampsia, there was but 1 of chronic pyelonephritis. The fact that, in a large group of patients with toxemia, acute "pyelitis" frequently occurs does not necessarily indicate a causative correlation between the two conditions. Thus in our experience bacteriuria occurred in 20 per cent of the normal pregnancies. The syndrome of toxemia and the characteristics of its hypertension are different from those of pyelonephritis. Toxemia superimposed on chronic pyelonephritis is therefore not a mere accentuation of the pre-existing hypertension, but represents the development of another morbid state, which frequently occurs without previous hypertension or renal disease.

PYELONEPHRITIS AND BRIGHT'S DISEASE

The fact that pyelonephritis can lead not only to renal failure, but also to vascular lesions and to arterial hypertension long after the disappearance of bacterial infection, indicates that in its chronic or healed stage it should be considered as one form of Bright's disease. Although acute pyelonephritis is the most frequent disease of the kidney, chronic pyelonephritis and diffuse healed pyelonephritis are also important renal diseases. Their relative role can be estimated from an analysis of 55 cases with small contracted kidneys. In this group the etiology of chronic Bright's disease was nephrosclerosis in 27 cases, pyelonephritis in 18 and glomerulonephritis in 10. Thus pyelonephritis is

oftener responsible for small contracted kidneys than is glomerulonephritis.

TREATMENT

The principle involved in the treatment of pyelonephritis necessitates the application of measures to relieve or improve stasis of the urinary flow in any part of the tract from the glomerulus to the urethra, and to interfere with the growth or multiplication of the causative organisms. In many cases the *chemical agent* used simply acts indirectly to intensify the immunologic reactions in the blood and tissues. The reaction of organisms to chemical substances in vitro does not justify conclusions as to their clinical efficacy. Many erroneous statements as to the value of urinary antiseptics have been based on such faulty assumptions. Thus mandelic acid is a bactericidal and a relatively better bacteriostatic agent than sulfanilamide for *Esch. coli* in vitro; and yet the latter is often more effective in the treatment of acute pyelonephritis caused by *Esch. coli*.

The natural history of pyelonephritis indicates that to be effective treatment should be instituted in the early acute stage of the disease. Not only do the progressive structural changes create a more favorable habitat for the bacteria, but in the subacute and in the chronic stage the surgical and chemical measures become less effective. Further, once the infection has reached a certain stage, the inflammatory tissue reactions often continue to advance long after the organisms have been eradicated. Thus hypertensive Bright's disease frequently develops during the bacteria-free stage.

Cases of successful abolition of arterial hypertension following *surgical removal of unilaterally diseased kidneys* are appearing in increasing numbers, but the follow-up period of the cases operated on is too short to warrant a final expression of opinion. It should be emphasized that the clinical diagnosis of unilateral renal ischemia is difficult. Systematic clinical study of the size and physiologic state of both the kidneys and the urinary passages is essential before surgical operation is undertaken. Mistaken diagnoses and inadequate consideration have been responsible for many fatalities.

Although in recent years great advances have been made in the study of pyelonephritis, this very progress has raised several new problems. Whereas it is recognized that the colon bacillus and the staphylococcus are the commonest causes of bacterial infection of the kidneys, a number of other bacteria may induce suppurative renal processes. Streptococcal infections often predispose to the subsequent development of *Esch. coli* pyelonephritis. At times, however, these and other bacteria

are found in the urine without pyuria. Are these cases of "silent bacteriurias" benign, or can they cause subsequent hypertension or renal failure? Should they be treated as intensely as those associated with the clinical picture of pyelonephritis? What are the factors that predispose one patient and not another to severe vascular lesions and hypertension? Are the renal vessels of some persons inherently more resistant to inflammatory tissue reaction than those of others? These and other questions cannot be answered at present.

SUMMARY

The clinical course of pyelonephritis varies considerably. Whereas in most cases the disease is benign and self-limiting, at times it becomes chronic, leading to arterial hypertension and to renal or cardiac insufficiency.

Pyelonephritis has been classified in four groups: acute (pyelitis), chronic (active), healed and healed with recurrence.

Two cases are reported as instructive examples of the natural history of pyelonephritis and of the relation of urinary-tract infections to the development of arterial hypertension. In Case 1 the renal infection started when the patient was six months old, and persisted until her death at the age of fifteen years. Although the local symptoms with pyuria dominated the clinical picture in early childhood, Bright's disease with arterial hypertension was the presenting syndrome during the last two years. The cause of death was uremia. In Case 2 healed pyelonephritis with recurrence caused by *Esch. coli* started during pregnancy at the age of twenty-five, and for twenty years there-

after numerous attacks occurred, leading to severe hypertension and angina pectoris.

Tuberculosis of the kidneys, infections of the renal pelvis, hydronephrosis and cystitis are usually not responsible for arterial hypertension.

Children with low-reserve kidneys of years' duration caused by pyelonephritis may have disturbances of bone formation with deformities (renal rickets), but the characteristics of these changes differ from those of true rickets.

Acute pyelonephritis (pyelitis) per se is usually not responsible for toxemia of pregnancy. It has an indirect relation to toxemia and eclampsia so far as it predisposes to arterial hypertension and to low-reserve kidneys.

Diffuse pyelonephritis in its chronic or healed stage should be considered as one form of Bright's disease.

The principles involved in the treatment and prevention of pyelonephritis are discussed.

REFERENCES

- 1 Wagner E. *Handbuch der Krankheiten des Harnapparates*. Part I. *Der Morbus Brightii*. 352 pp. Leipzig, F. C. W. Vogel, 1882.
- 2 Göppert F. Ueber die eitrigen Erkrankungen der Harnwege im kindesalter Pyelitis Pyelocystitis und Cystitis. *Ergebn d inn Med u Kinderh* 2:30-73, 1908.
- 3 Longcope W. T., and Winkenwerder, W. L. Clinical features of the contracted kidney due to pyelonephritis. *Bull Johns Hopkins Hosp* 53:255-287, 1933.
- 4 Peters J. P., Laviettes P. H., and Zimmerman H. M. Pyelitis in toxemias of pregnancy. *Am J Obst & Gynec* 32:911-927, 1936.
- 5 Weiss S., and Parker, F., Jr. Pyelonephritis: its relation to vascular lesions and to arterial hypertension. *Medicine* 18:221-315, 1939.
- 6 Addis T., and Oliver J. *The Renal Lesion in Bright's Disease*. 628 pp. New York: Paul B. Hoeber, 1931. P. 64.
- 7 Mallory, G. K., Crane A. R., and Edwards J. E. Pathology of acute and of healed experimental pyelonephritis. *Arch Path* 30:330-347, 1940.
- 8 Parker, F., Jr., and Weiss S. The nature and significance of the structural changes in the lungs in mitral stenosis. *Am J Path* 12:573-598, 1936.
- 9 Weiss S., Dexter, L.; Parker, F. Jr., and Tenney, B. Arterial hypertension in pregnancy and the hypertensive toxemia syndrome of pregnancy (preeclampsia and eclampsia). *Tr A Am Physicians* 55:282-288, 1940.

OPEN-AIR SANATORIUM CARE FOR PATIENTS WITH RHEUMATIC FEVER AND RHEUMATIC HEART DISEASE*

Preliminary Report

JOHN P. HUBBARD, M.D.,† AND WALTER A. GRIFFIN, M.D.‡

BOSTON

THE purpose of this paper is to review briefly, as a preliminary report, the experience of two years in caring for a small group of children with rheumatic fever in an open-air sanatorium in the rigorous climate of Boston. This has been an experiment, arising from the facts, increasingly apparent, that rheumatic fever is widespread among undernourished children crowded together in unhealthy environments and that provision for their care is altogether inadequate.

THE EXPERIMENT

In the fall of 1938, at the suggestion of Dr. Kenneth Blackfan, the Sharon Sanatorium, which is just outside Boston, made available for the care of children with rheumatic fever a pavilion previously used as a preventorium for tuberculosis. The capacity of the building is ten boys and ten girls. The children have been selected from the Children's Hospital. Their placement has been financed in part by The Children's Mission to Children and in part by the sanatorium. Primarily this has been an experiment in hospitalization based on an attempt to determine whether a rheumatic child in a carefully controlled, open-air environment can be kept free of respiratory infections, and whether the infection itself responds favorably to such an environment.

During the winter of 1938-1939, 20 children who had recently recovered from active rheumatic fever were sent to the sanatorium. Whenever possible, they were admitted following the first attack. Some had respiratory infections at the time of admission, but all were free from active rheumatic infection. They entered in the fall and remained as a closed colony during the winter and spring months. There was careful restriction in regard to visitors. Only the child's parents were allowed to visit, one afternoon a week. All visitors were required to wear masks, and no one with a cold, sore throat or other infection was permitted near the building. Emphasis was placed on education of the children, so that on returning

home they were able to continue with their proper grades in school. A full-time occupational therapist was available to keep them happy and busy when they were not at their schoolwork. The children slept outdoors, even in the severest weather, and were kept in the open air as much as possible during the day.

Throughout the winter all the children remained free from respiratory infections, and recurrences of rheumatic fever (Fig. 1). During the summer of 1939, 15 children were discharged, the rest being kept for further care. The discharged children have been followed by the Rheumatic Fever Clinic at the Children's Hospital for an average period of over a year. Since returning home from the sanatorium, some of them have developed respiratory infections and other minor ailments, but none have had recurrences of rheumatic fever or evidence of increased heart disease.

With this experience as a background, a change in policy was made during the following winter. Only children with active rheumatic infection were placed. Some of them had rather severe rheumatic fever and heart disease. Furthermore, the policy of maintaining a closed colony was abandoned, and children were admitted as beds became available. The only restrictions in the selection of patients were that they should have well-established disease, and be between the ages of five and twelve years, free from chorea and free from heart failure. These restrictions were considered necessary because of the limited nursing service and, in the case of heart failure, because of limited medical supervision.

During the second year 28 children were admitted. The course of their disease was followed by clinical observation, more specifically by that of temperature, sleeping pulse rate and gain in weight, and determinations of the erythrocyte-sedimentation rate. When shown to be free of all evidence of active infection, they were allowed a gradual increase in activity for two months, when they were permitted full activity. Instead of being sent home at this time, they were kept for a further period of a few months, during which it was hoped that they would overcome any latent rheumatic infection and attain a state

*From the Children's Hospital, the Department of Pediatrics, Harvard Medical School, and the Children's Mission to Children, Boston, and the Sharon Sanatorium, Sharon, Massachusetts.

†Instructor in pediatrics, Harvard Medical School; associate physician, Children's Hospital.

‡Medical director, Sharon Sanatorium.

of vigorous health, to enable them to withstand the rigors of their home environment, which was probably poor at best.

The results during the second year were as completely satisfactory as those during the first. During the second winter the children remained free of respiratory infections except for one or two minor head colds. Of greater significance was the absence of recurrent rheumatic infection in any case (Fig. 2). This was all the more gratifying

Another feature that has most impressed those who have watched these children from week to week is their steady uninterrupted gain in general health. This is difficult to demonstrate with factual data. It is reflected in part by their gain in weight, which is a sign that convalescence is progressing satisfactorily (Fig. 3).

During the second year, to study further the factors that might have contributed to the freedom from infection within the group, cultures were

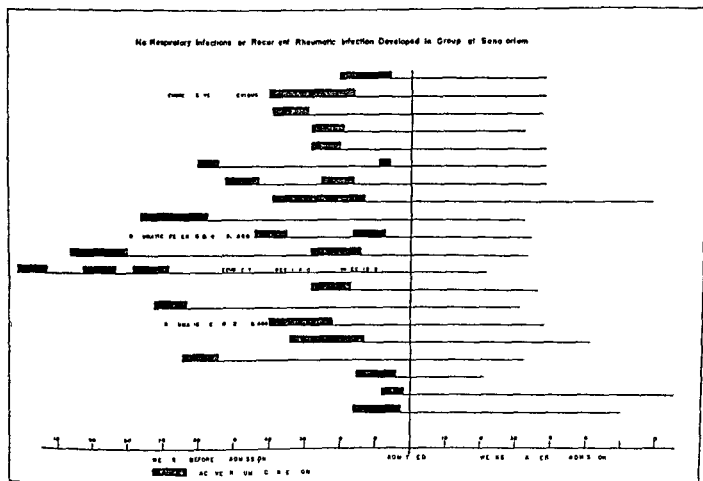


FIGURE 1

The courses of the first 20 rheumatic children at the sanatorium showing periods of active infection before admission, freedom from active infection on admission, and freedom from active infection following admission.

because the children had varying degrees of active infection on admission, and hence were sicker than those in the first group, who had already recovered from their active infection.

As stated above, children with congestive heart failure have not been considered suitable for the present facilities of the sanatorium. In one child heart failure developed between the time she was accepted at the clinic and her admission. She represented the overwhelming, rapidly progressive form of rheumatic heart disease, from which she died after having been sent back to the hospital. Obviously no claim is made that a progressive course such as this can in any way be influenced by one form of hospitalization in contrast to another. This in no way detracts from the value of the sanatorium experience, the essential feature of which is the freedom, to date, from respiratory infection and recurrent rheumatic fever.

taken regularly from the children's throats and repeatedly from samples of the air. A considerable number of hemolytic streptococci have been obtained from the throat cultures, since the typing of these is not finished, the results are not reported here, but will be included in a more complete presentation of this work at a later date. The cultures of the air have been helpful in giving bacteriological evidence to support the value of the open air environment. With freely circulating air that is rapidly diluted with the outer air there is relative freedom from bacterial contamination in comparison with the usual hospital wards. This is illustrated by Figure 4, which is taken from the work of Fe del Mundo and McKinnon.¹ By means of the Wells² centrifuge apparatus, estimations have been made of the number of bacteria per 10 cubic feet of air. Repeated determinations were made during the winter, spring and summer under

varying conditions. The bacterial counts obtained in this manner compared favorably with similar counts obtained in a very carefully supervised, air-conditioned, infection-free premature nursery and in infant cubicles protected with ultra-violet radiation. The counts taken from hospital wards and waiting-rooms showed a much greater bacterial contamination. Also of considerable significance is

value of these factors. In the meantime, this type of care deserves continued trial, particularly since the very real problem of the most suitable management for the rheumatic child is now receiving considerable attention. Appreciation of this problem has resulted, on the one hand, from an increasing recognition of the prevalence and severity of the disease, and on the other, from a growing

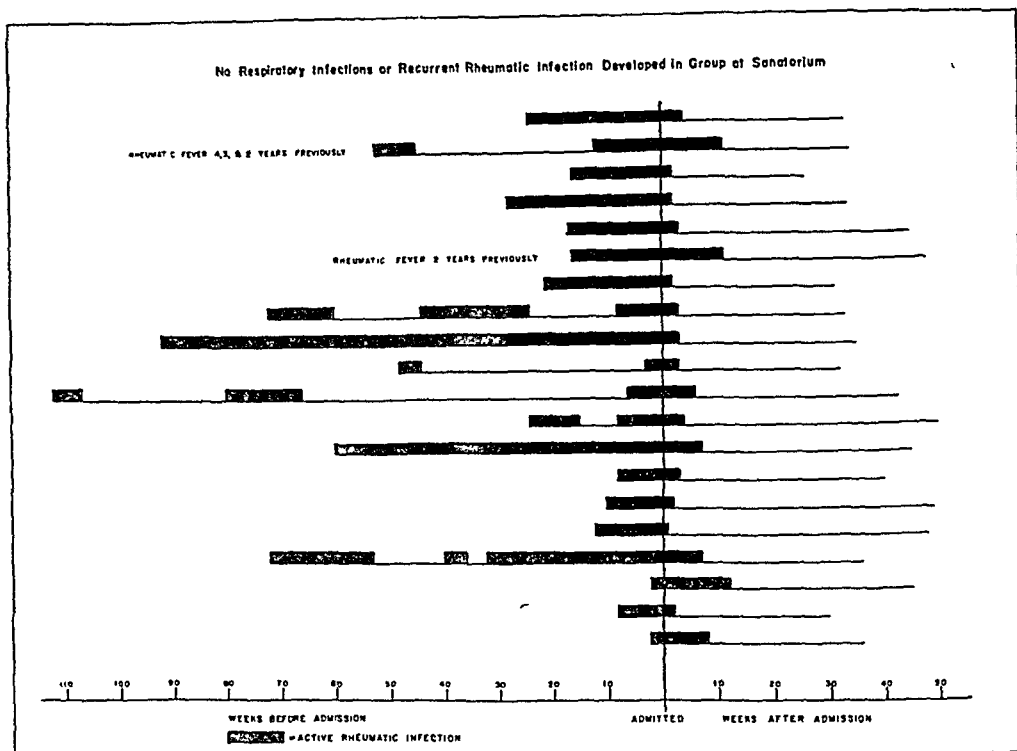


FIGURE 2.

The courses of the second 20 rheumatic children at the sanatorium, showing active infection before and on admission and freedom from active infection following admission.

the fact that hemolytic streptococci and other pathogenic bacteria were found in the samples from the hospital wards, whereas only staphylococci, molds and a variety of nonpathogenic organisms were obtained at the sanatorium.

DISCUSSION

It would be premature at present to attempt to analyze too closely the results of this experiment. The time has been short, and the number of cases limited. Many features must be further analyzed. Among these may be mentioned the open-air environment, the small size of the group, the strict control of visitors, the small personnel coming in contact with the children, the optimal diet and the careful regulation of the activities of each child. Rheumatic fever being a chronic and recurrent disease, it will probably be several years before conclusive statements can be made in regard to the

realization of the lack of facilities now available for its proper care.

The incidence of rheumatic fever is difficult to determine, since it is not a reportable disease and hence does not appear in the community vital statistics. Recently in Boston a laborious case-finding study³ revealed that 900 new cases of rheumatic fever, or rheumatic heart disease, occur each year within the city limits. For the same period and in the same area, there were 878 new cases of pulmonary tuberculosis.⁴

The severity of the disease is made all too apparent by the frequency with which it causes heart damage or death. Bland and Jones⁵ have shown that in a series of 1000 cases followed for an average of over ten years, 426 patients had varying degrees of heart disease and an additional 243 died. From this experience it can be assumed that of the 900 new patients each year, most of whom

are children, 400 may be expected to be left with heart disease, many permanently crippled, and over 200 may be expected to die within ten years.

Similar mortality statistics have been published from Philadelphia,⁶ a community comparable to Boston in the incidence of rheumatic fever. During 1936, 357 deaths were reported as certainly

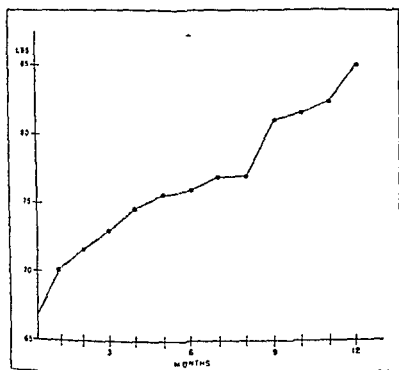


FIGURE 3.

Composite weight chart of the first 40 rheumatic children, showing the gain while at the sanatorium.

and 195 as probably due to rheumatic heart disease. Among persons under twenty years of age, rheumatic heart disease caused more deaths than did whooping cough, measles, meningococcal men-

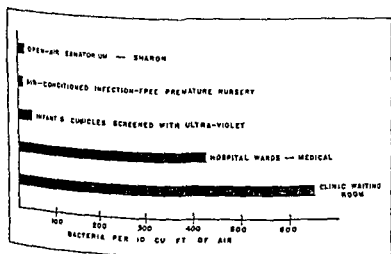


FIGURE 4.

Bacterial contamination of air at the sanatorium in comparison with an air-conditioned, infection-free nursery, infants' cubicles screened with ultra-violet light, hospital wards and waiting room (Fé del Mundo and McKhann¹).

ingitis, diphtheria, scarlet fever and poliomyelitis combined.

There is reason to believe that carefully controlled, prolonged bed rest may have some bearing on the ultimate outcome for the individual case.

At any rate, it is generally agreed that the rheumatic patient should be restricted to bed so long as there is any evidence of active infection, and should then have a further period of months of carefully regulated increasing activity. The duration of convalescent care is therefore comparable to that for tuberculosis. There are in Massachusetts over 4000 beds provided for patients with tuberculosis,⁷ but only 177 for those with rheumatic fever.³

England has taken the lead in accepting the community responsibility for the care of rheumatic fever.⁸ In London, it was recognized some years ago that the problem was too urgent and too extensive to be dealt with entirely by private or charitable organizations. The Ministry of Health therefore took active steps in the matter, the result being the provision of over 1000 beds for rheumatic children in the London area and an annual expenditure of over £220,000.

That the cause of rheumatic fever is still in doubt is a factor that has hampered progress in the care of patients. However, what we do know offers an approach to the problem. It is, for example, increasingly clear that there is a close relation between rheumatic fever and hemolytic streptococcal infections of the nose and throat.⁹⁻¹¹ Not only do such infections precede the initial attack of rheumatic fever, but they may also reactivate the infection during its convalescent stages. Every reappearance of the disease increases the likelihood of damage to the heart. Furthermore, when heart disease has already occurred, recurrences increase its severity and the chances of an early death. In Wilson's¹² series the mortality increased from 20 per cent when there had been only one attack to 64 per cent after four or more.

Prevention of colds and sore throats, therefore, becomes of the utmost importance for the rheumatic patient, and should be the criterion of any plan of hospitalization. This consideration has prompted transportation of these patients to a tropical climate where both respiratory diseases and rheumatic fever are less prevalent. Groups of children have been sent from Boston to Florida,¹³ from New York to Puerto Rico¹⁴ and from other places to Arizona.¹⁵ The results have been disappointing. Some of the children sent to Florida¹⁶ improved in the tropical environment, several had recurrences of rheumatic fever, and a few died. When the patients returned home they had little resistance to further infections. In other words, the tropical sojourn appeared to do no permanent good. Furthermore, from the economic point of view such a plan is impractical, since most of the rheumatic patients come from families with low incomes.

The method of caring for the children in small groups in an open-air sanatorium, although a rather different approach to the problem, has also been based primarily on an attempt to control respiratory infections within the group. In comparison with any transportation plan, it has the advantage of keeping the child in the sort of climate in which he will probably have to live, causing much less disruption of the family and being reasonable in cost. Furthermore, the child returns to his home in robust health, with increased resistance to the infections of his crowded home and school life. In short, the plan appears reasonable and has, during a preliminary period of two years, met with success.

SUMMARY

During two years nearly 50 rheumatic children have been cared for in an open-air sanatorium, with excellent results. There was freedom from respiratory and recurrent rheumatic infection. The children showed a steady and uninterrupted gain in general health. These results are particularly encouraging in the light of the rather severe weather during the second winter and the accompanying prevalence of streptococcal infections and recurrent rheumatic fever in other hospital groups and elsewhere throughout the community.

Until further experience has been accumulated, it is unnecessary and unwise to attempt a close analysis of the various factors that may have contributed to the success of this enterprise. However, this type of treatment is rational and economically sound, and on the basis of experience to date deserves further trial.

REFERENCES

- 1 del Mundo, F., and Mchhann, C. F. Ultra violet radiation in control of hospital infections in an infants' hospital. *Am. J. Dis. Child* (in press)
- 2 Wells, W. F. Apparatus for study of bacterial behavior of air. *Am. J. Pub. Health* 23:58, 1933
- 3 The Children's Mission to Children, Boston, personal communication
- 4 Sixty seventh Annual Report of the Health Department of the City of Boston for the Year 1938. 170 pp. Boston: City of Boston Printing Dept., 1939. P. 160
- 5 Bland, E. F., and Jones, T. D. Fatal rheumatic fever. *Arch. Int. Med.* 61:161-171, 1938
- 6 Hedley, O. F. Mortality from rheumatic heart disease in Philadelphia during 1936. *Pub. Health Rep.* 52:1907 1923, 1937
- 7 Massachusetts Department of Public Health, Division of Tuberculosis, personal communication
- 8 Schlesinger, B. Public health aspect of heart disease in childhood. *Lancet* 1:593 599, 649 654, 1938
- 9 Jones, T. D., and Mote, J. R. The clinical importance of infection of the respiratory tract in rheumatic fever. *J. A. M. A.* 113:898 902, 1939
- 10 Coburn, A. F., and Pauli, R. H. Studies on the immune response of the rheumatic subject and its relationship to activity of the rheumatic process. *J. Exper. Med.* 62:129 178, 1935
- 11 Coburn, A. F. Observations on mechanism of rheumatic fever. *Lancet* 2:1025 1030, 1936
- 12 Wilson, M. G. *Rheumatic Fever*. 595 pp. New York: The Commonwealth Fund, 1940. P. 249
- 13 Roche, C. F., and Jones, T. D. Heart disease of the rheumatic type. *J. Florida M. A.* 20:342 346, 1934
- 14 Coburn, A. F. *The Factor of Infection in the Rheumatic State*. 288 pp. Baltimore: Williams & Wilkins Co., 1931
- 15 Tappan, V. discussion of Shapiro, M. J. Diagnosis of rheumatic fever. *J. Pediat.* 14:400 413, 1939
- 16 Jones, T. D. unpublished data.

THE TREATMENT OF PEPTIC ULCER WITH ALUMINUM HYDROXIDE: A TWO-YEAR STUDY*

S. ALLEN WILKINSON, M.D.,† AND PETER D. COMANDURAS, M.D.‡

BOSTON

THE treatment of peptic ulcer without complications is primarily medical. This principle is accepted today by an overwhelming majority of workers in this field. Such treatment, in addition to diet, rest and other usual hygienic measures, includes the reduction and, if possible, complete neutralization of hydrochloric acid in the stomach by means of various alkali substances. The second method has apparently not received the complete and wide approbation that has been accorded the first. We shall not present a detailed discussion of the importance or mere coincidental appearance of the acid factor in peptic ulcer. We have aligned ourselves, however, with those who believe that "one cannot discard the idea of acid and its effects on ulcer without coming to an impasse."¹ The

unequivocal relation that acid bears to the problem of peptic ulcer rests on the foundations of experimental and clinical medicine. Experimental evidence, notably the work of Mann and Williamson,² Dragstedt³ and others, has shown that the production of duodenal ulcers in dogs, the prevention of healing of these ulcers and their probable recurrence after healing are phenomena intimately associated with the unneutralized presence and unhampered activity of free acid in the stomach. Modern surgical endeavors are directed toward the removal of as large an acid-bearing area of the stomach as possible, and the consequent reduction of free acid to as low a level as possible. Lahey⁴ expresses the trend of thought of many Continental and American surgeons when he says: "There seems little question that the best surgical results, immediate and remote, are in those ulcer patients who postoperatively have a very low gastric acid or gastric anacidity." Furthermore, Ivy⁵ states that

*From the Department of Gastroenterology, Lahey Clinic

†Member, Department of Gastroenterology, Lahey Clinic

‡Formerly, fellow in gastroenterology, Lahey Clinic; assistant gastroenterologist, Joseph H. Pratt Diagnostic Hospital and Massachusetts Memorial Hospitals

although "it cannot be proved that gastric juice is the factor initiating peptic ulcer, much evidence indicates that unneutralized gastric juice is an important if not a prime factor contributing to the chronicity of peptic ulcer."

Consequently, if we accept the principles that treatment of peptic ulcer is primarily medical and that such treatment should be substantially the inactivation of acid in the stomach, it perforce becomes a matter of distinct urgency to study and evaluate the effectiveness of the numerous neutralizing substances offered to the profession. Since the results for the first six months of the medical treatment of peptic ulcer are usually excellent, no matter what method is used, we decided to study the effectiveness of these antacids over a longer period.

This investigation, then, was undertaken with the express purpose of subjecting to a thorough study, covering a period of two years, the various antacids used in the Lahey Clinic for the reduction of gastric acidity in proved cases of peptic ulcer. We shall not concern ourselves with the subjective improvement of these patients, but shall confine our efforts to determining which of the various substances has been most effective over a two-year period.

Although this study deals primarily with the effects of various neutralizing agents, principally Sippy powders and aluminum hydroxide, as neutralizing agents after a prolonged period of use, it is of interest to note that clinically the results of treatment were approximately the same whichever of these two agents was employed. Whether some difference will develop after a longer follow-up period in the cases which still have a high acid level, principally those treated with Sippy powders, as against those which have shown a marked reduction in acid, principally those treated with aluminum hydroxide, remains to be determined. In a later paper we shall discuss the subjective and clinical improvement of patients under different types of medication over a long period of time. As a matter of fact, clinical results and subjective improvement depend so much on variables other than the type of medication used that it is difficult to evaluate the efficacy of any particular medication in the treatment of ulcer solely on this basis.

We reviewed the clinical records of 730 cases of peptic ulcer admitted between January, 1936, and January, 1938. This number constituted 3.4 per cent of the total admissions. There were 705 cases of duodenal ulcer, 14 of gastric ulcer, and 11 of jejunal ulcer. The sex ratio was 3 males to 1 female, in both duodenal and gastric ulcer cases.

In the 11 jejunal ulcer cases, however, 10 patients were males. The youngest patient, seventeen years old, and the oldest, eighty-two, were both males. Two thirds of both males and females were between thirty and fifty-nine years of age.

For the purposes of this report we were able to utilize 308 cases. The others could not be included, because of insufficient data, incomplete study, questionable diagnosis or inadequate treatment.

Fourteen hundred gastric analyses were performed in the 308 cases, of which only 521 could be included in this report. Of these, 263 (50 per cent) were made following the use of Sippy powders exclusively, 159 (30 per cent) following the use of aluminum hydroxide exclusively, and the rest (20 per cent) following the use of mixtures and proprietary remedies.

It should be emphasized that these determinations of gastric acidity were done with an unvarying procedure throughout the study. Only those figures were used that were obtained after a standard Ewald test meal, given on a fasting stomach and aspirated forty-five minutes after the meal. No alkalis of any kind had been administered during the preceding twelve hours. Therefore, the figures obtained should indicate the functioning response of the gastric glands to the test meal without benefit of neutralizing agents. The determinations listed here are those of free hydrochloric acid, and are expressed as the number of cubic centimeters of N/10 sodium hydroxide required to neutralize 100 cc. of gastric juice.

The efficacy of Sippy powders in promptly neutralizing the stomach acidity when given in adequate doses is readily admitted. However, in the course of endeavors to neutralize completely the free hydrochloric acid, symptoms of toxemia and alkalosis develop in a considerable number of patients. It has also been observed that patients with ulcer and renal insufficiency, hepatic cirrhosis, arteriosclerosis or hypertension are markedly susceptible to alkalosis. Furthermore, an objectionable feature of the sodium bicarbonate in the Sippy powders has been the tendency for the acid content to return to higher levels following their use. Consequently, many neutralizing substances have been offered that allegedly provide adequate neutralization without the associated ill effects of toxemia and alkalosis. One of these that has received wide use and approval is aluminum hydroxide. Original papers by Crohn,⁶ Rowland and his associates,^{7,8} and Jones⁹ have expressed favorable opinions of the value of this substance. It is claimed that it combines with hydrochloric acid to form aluminum chloride and that no matter how much is given, an alkaline reaction cannot be produced,

because of its amphoteric qualities. In the small intestine, the biliary and pancreatic secretions react with it to re-form sodium chloride and re-precipitate aluminum hydroxide. It is therefore claimed that colloidal aluminum hydroxide can act as an efficient neutralizer of gastric acidity, is nonabsorbable and is thus incapable of producing alkalosis.

Acid determinations were made at periods of three, six, nine, twelve and twenty-four months in order to ascertain what changes, if any, occurred at these times as compared with the gastric analysis made on the first admission. An increase in acidity was taken to mean one of 20 units or over; a decrease to mean one of 20 units or over, and little or no change to mean an alteration of not more than 19 units in either direction.

As shown in Table 1, at the end of three and six months following the use of aluminum hydroxide there was a decrease in gastric acidity in 42

TABLE 1. *Deviations from Original Acid Level in 308 Cases.*

No. OF MONTHS OF TREATMENT	DECREASE		NO CHANGE		INCREASE	
	SIPPY POW-DERS	ALUMINUM HYDROX-IDE	SIPPY POW-DERS	ALUMINUM HYDROX-IDE	SIPPY POW-DERS	ALUMINUM HYDROX-IDE
	%	%	%	%	%	%
3	27	42	58	48	14	10
6	19	45	74	40	7	15
9	20	42	65	47	15	11
12	25	52	59	44	16	4

and 45 per cent of the determinations, respectively, whereas following the use of Sippy powders there was a decrease in only 27 and 19 per cent, respectively. At the end of nine and twelve months following the use of aluminum hydroxide there was a decrease in acid in 42 and 52 per cent, respectively, of the determinations, whereas following the use of Sippy powders there was a decrease in only 20 and 25 per cent, respectively.

Thus, throughout the first year, aluminum hydroxide produced a decrease in gastric acidity in over 40 per cent of determinations, and was apparently twice as effective as Sippy powders in reducing acidity. Also, a slightly smaller percentage of aluminum hydroxide determinations showed an increase in gastric acidity at each of these monthly periods, except at the end of the six-month period.

Another development noted was the effectiveness of aluminum hydroxide in reducing gastric acidity as much as 40 and 50 units from the original acid level. Following the use of Sippy powders, only 8 acid determinations were reduced 40 units, and none 50 units. Following the use of aluminum hydroxide, however, 30 determinations showed the acidity as reduced 40 and 50 units.

These findings are interesting because there were more determinations following the use of Sippy powders than following aluminum hydroxide therapy. Certainly, the effectiveness of aluminum hydroxide in controlling acidity even over a long period of time is well demonstrated (Table 2).

To test the effectiveness of these neutralizers still further, it was decided to study 63 cases in which complications were present. In these cases

TABLE 2. *Cases Exhibiting a Maximum Decrease in Gastric Acidity.*

No. OF MONTHS OF TREATMENT	40-UNIT DECREASE		50-UNIT DECREASE	
	SIPPY POW-DERS	ALUMINUM HYDROXIDE	SIPPY POW-DERS	ALUMINUM HYDROXIDE
3	1	6	0	5
6	0	1	0	2
9	0	3	0	2
12	0	2	0	3
24	0	0	0	1

medical treatment had admittedly been unsatisfactory, and there was an urgent necessity to reduce gastric acidity as much as possible, to provide healing of tissue and prevent chronicity and further inroads of the disease.

There was a history of recent hemorrhage in 21 cases; obstruction was present in 14; 7 patients had had a gastroenterostomy, 4 of whom had gastrojejunal ulcer on admission. The 21 remaining cases had various other complications among which may be listed 5 cases each with diaphragmatic hernia and with duodenal diverticula, 2 with gallstones, 2 with associate gastric ulcers, 1 with perforation, 2 with thyroid disease and 3 with renal stones.

From the records, we were able to list 82 acid determinations following the use of Sippy powders and 38 following that of aluminum hydroxide. The latter produced a decrease of 20 units or over in gastric acidity in 48 per cent of all determinations, whereas the former resulted in a decrease in only 17 per cent. This is additional evidence to show that even in ulcer cases with complications, in which neutralization is so important, aluminum hydroxide seems to be twice as effective in reducing gastric acidity as are Sippy powders.

Remembering that the longer the duration of symptoms in these ulcer cases, the less favorable becomes their response to medical treatment, we thought that a study of those cases in which the duration of symptoms was over twenty years would prove enlightening. There were 30 such cases in the series, of which only 12 could be used for the purposes of study. There were complications in half these cases, the average age was fifty-eight and the average duration of symptoms was thirty years, all these factors being definitely unfavorable

so far as response to medical therapy and neutralizers is concerned. In the 23 acid determinations, 6 of the 7 cases receiving aluminum hydroxide showed a decrease of 20 units or more, whereas only 2 of the 5 receiving Sippy powders showed such a decrease.

CONCLUSIONS

The neutralization of gastric acidity is an integral part of the medical treatment of peptic ulcer.

The results of a two-year study covering the comparative neutralizing effectiveness of two antacid substances, Sippy powders and aluminum hydroxide, in reducing gastric acidity are presented.

Following the use of aluminum hydroxide 40 per cent of the acid determinations at the end of three, six, nine and twelve months showed a reduction in gastric acidity of 20 units or over. Following the use of Sippy powders, only approximately 20 per cent of the determinations showed such a decrease.

There were more than three times as many reductions of 40 and 50 units and over following

the use of aluminum hydroxide than there were following the use of Sippy powders.

In the cases with severe complications and in those with a duration of twenty years and over, aluminum hydroxide also showed greater effectiveness in reducing acidity than did Sippy powders.

SUMMARY

In a study of 308 cases of peptic ulcer, reviewing 521 gastric analyses, it was found that aluminum hydroxide is a much more effective neutralizer over a long term period than are Sippy powders.

REFERENCES

- 1 Crohn B B. *Affect on of the stomach*. 907 pp. Philadelphia: W B Saunders Co. 1922. P. 538.
- 2 Mann F C and Williamson C S. Experimental production of peptic ulcer. *Ann Surg* 77:409-422 1923.
- 3 Dragsted L R and Vaughn A M. Gastric ulcer studies. *Arch Surg* 91:810 1924.
- 4 Laker F H. Peptic ulcer gastric duodenal and jejunal. *S Clin North Amer* 15:1401-1413 1935.
- 5 Ivy A C. Application of recent contributions in basic medical sciences to surgical practice. *Internat Abstr Surg* 66:18 1938.
- 6 Crohn B B. The clinical use of colloidal aluminum hydroxide as a gastric antacid. *J Lab and Clin Med* 14:610-614 1919.
- 7 Wollman E E and Rowland V C. A new technique for the continuous control of acidity in peptic ulcer. *Am J Digest Dis and Nutr* 2:33-36 1936.
- 8 Emsell I H and Rowland V C. The aluminum hydroxide treatment of peptic ulcer. *Ohio State M J* 28:173 1932.
- 9 Jones C R. Jr. Colloidal aluminum hydroxide in the treatment of peptic ulcer. *Am J Digest Dis and Nutr* 4:99-107 1937.

THE REACTION OF LEUKEMIC PATIENTS TO SULFAPYRIDINE ADMINISTRATION*

A Preliminary Report

KENNETH E. LIVINGSTON M.D.,† AND RUTH D. MOORE B.S.‡

BOSTON

NUMEROUS reports¹⁻⁶ in the recent literature refer to the leukopenia due to sulfapyridine and related drugs, but we know of no study reporting their effects on patients with leukemia. This paper concerns observations on the reaction of 9 such patients to the administration of sulfapyridine. The first observations were made on a patient (Case 1) who had received routine x-ray therapy. A few days later he developed lobar pneumonia and was given sulfapyridine. The changes in the white-cell count during this period led to the investigation.

CASE 1. W.B. (H.M.H. 39 1003) a 70-year-old man, entered the hospital on August 7, 1939, with symptoms of 1 year's duration that were typical of chronic lymphatic leukemia. The white-cell count was 256,000 with 90 per cent lymphocytes and 8 per cent lymphoblasts. The patient received 1000 r (1000 kv.) of x-ray therapy. The

white cell count was falling 4 days after the last x-ray treatment when the patient developed lobar pneumonia (Type 14). He was given sulfapyridine in routine dosage. The drug was discontinued after 48 hours because the white cell count had reached 7100. The pneumonic process did not clear, although the patient was afebrile for 4 days. On the 5th day he had a sudden chill with clinical evidence of active pneumonia in the same area. The patient was again given sulfapyridine, but in restricted dosage. During the following 4 days the white-cell count fell from 10,850 to 6500, and then rose slowly after the drug was withdrawn. Because of the possibility that the sulfapyridine might bear some specific relation to the fall in the white cell count it was decided to study the patient's reaction to the drug in the absence of infection.

After 17 days the white-cell count had risen to 33,500. The patient received 5 gm. of sulfapyridine by mouth in a period of 12 hours. During the following 32 hours the white-cell count fell to 11,000. The patient was discharged to the Outpatient Department.

Twenty-one days later the patient's reaction to the drug was again studied. The white-cell count had risen to 47,000. The response to sulfapyridine is shown in Figure 1.

The patient was followed in the Outpatient Department for the next 2 months, during which the white-cell count

*From the Medical Laboratories of the Collis P. Huntington Memorial Hospital at Harvard University.

†Formerly research fellow in medicine, Harvard Medical School.

‡Formerly technician, Collis P. Huntington Memorial Hospital.

rose to 94,000. He was readmitted to the hospital and again given sulfapyridine. The response is shown in Figure 2. Six days after admission the patient was given a single intravenous dose of 5 gm. of the soluble sodium salt of sulfapyridine. At this time the lymph nodes were palpable but not grossly enlarged. Four hours after receiving this dose the patient complained of soreness in the region of the cervical and axillary lymph nodes. This increased during the night and required medication to control pain. Within 18 hours after sulfapyridine had been given, lymph nodes throughout the body were grossly enlarged, very tense, warm and tender to palpation. Forty hours after injection two cervical nodes were removed for study. One of these showed a large central focus of hemorrhage. A wet smear of the node before fixation

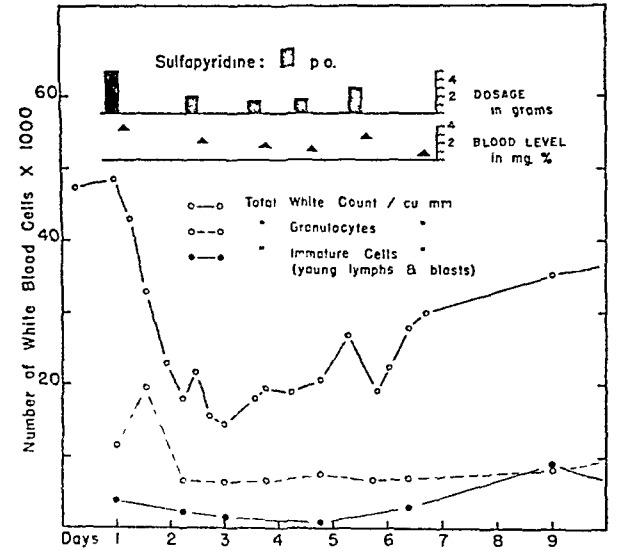


FIGURE 1. Case 1.

showed cells identical with the blast forms which had appeared in the peripheral blood smear within a few hours after the drug had been given by vein. Lymphoblasts, which had previously been rare in the circulating blood (0.0 to 2.0 per cent), rose to 10 to 14 per cent. It was believed that the drug in high concentration had produced cell destruction, particularly in the lymph nodes, and that the products of cell breakdown had led to an acute local inflammatory reaction. The patient was discharged to be followed in the Outpatient Department. At the time of discharge the white-cell count was rising. The enlarged nodes were obviously beginning to regress. It was not possible to determine accurately whether the spleen had shown a parallel fluctuation in size. The nodes returned to their former size in a period of 8 to 10 days.

CASE 2. J. H. (H. M. H. 39-1239), a 15-year-old school-boy, was first admitted to the Massachusetts General Hospital because of dyspnea of 12 days' duration. X-ray examination showed a large tumor mass in the mediastinum. Examination of a biopsied supraclavicular lymph node showed malignant lymphoma of the lymphoblastic type. The patient received 1300 r (200 kv.) of x-ray therapy to the chest. At the time of discharge the mediastinal shadow was considerably reduced and the patient's symptoms alleviated.

Five weeks after the patient's first symptoms, he was seen at this hospital. Examination of the blood showed a white-cell count of 15,200, with 52 per cent polymor-

nuclears, 10 per cent band forms, 19 per cent lymphocytes, 12 per cent monocytes, 1 per cent metamyelocytes, 3 per cent eosinophils and 2 per cent basophils. The platelets appeared to be reduced.

Two months after the onset of symptoms the patient was admitted to the hospital in a critical condition, with the picture of acute lymphatic leukemia. There was marked anemia, bleeding, slight lymph-node enlargement and a palpable spleen. The blood study showed a red-cell count of 2,530,000, with 55 per cent hemoglobin (Sahli). There was a white-cell count of 212,000, with 1.5 per cent polymorphonuclears, 0.5 per cent basophils, 1.5 per cent small lymphocytes, 3.0 per cent medium lymphocytes, 88.5 per cent atypical lymphocytes and 3.0 per cent blasts. The platelets appeared to be reduced. The patient was immediately given a transfusion of 350 cc., following which the white-cell count was 183,750. He was given sulfapyri-

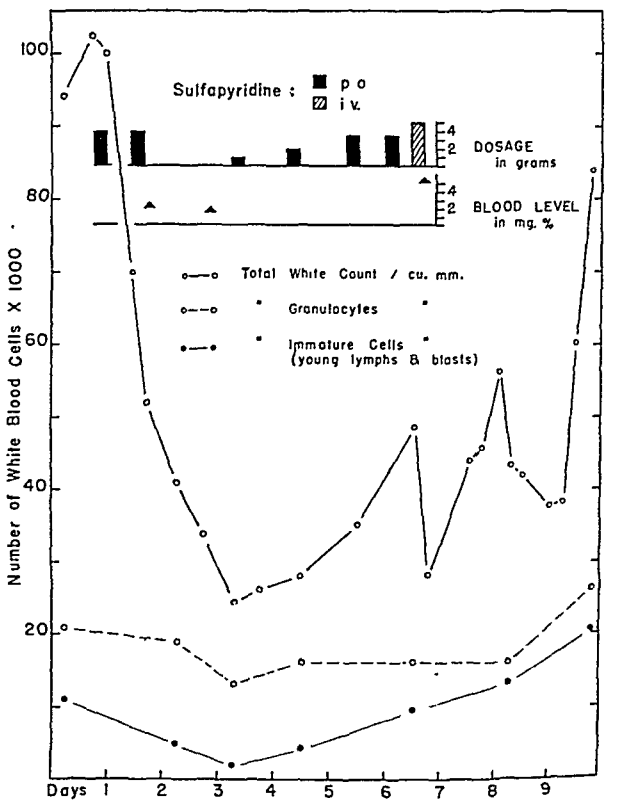


FIGURE 2. Case 1.

dine. Changes in the white-cell count, the dosage, the blood level of the drug and the transfusions are indicated in Figure 3. In addition to the marked change in total white-cell count, there was a distinct change toward maturity in the character of the cells. On the 19th day of treatment the drug was discontinued, because in spite of the change in blood picture there was clinical evidence of widespread leukemic infiltration.

CASE 3. E. F. (H. M. H. 35-481), a 60-year-old woman, was found on routine examination to have an asymptomatic chronic lymphatic leukemia, with a white-cell count of 59,000, with 85 per cent lymphocytes. This diagnosis was confirmed by examination of a biopsied supraclavicular lymph node. The patient required no treatment for the disease, since her general health was excellent. She was given a small dose of sulfapyridine by vein to determine

whether the drug would produce changes in the white cell count similar to those seen in Cases 1 and 2. In the 18 hours after she had received intravenously 25 gm of the soluble sodium sulfapyridine, the white-cell count fell to 29,000. Equal doses at 24 and 48 hours produced no further significant fall in the count. The patient was discharged with a white cell count of 26,100.

In addition, 6 other cases of leukemia have been studied. Case 4 (H M H 39-1429) and Case 5 (H M H 39-1341) were those of patients with chronic lymphatic leukemia. Both were given adequate doses of the drug, orally and intravenously, to attain high blood levels. Neither case showed

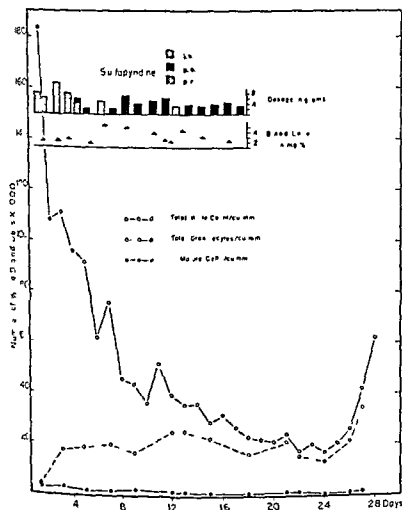


FIGURE 3 Case 2

a definite response. Examination of biopsied lymph nodes before and after treatment in Case 4 showed no significant microscopic change, although grossly there was obvious edema.

CASE 6* H L (P B B H 114080) was a 57-year-old patient with chronic lymphatic leukemia, whose reaction to the drug was observed during treatment for lobar pneumonia. The white-cell count on admission was 70,000. He was given sulfapyridine orally, and the blood level reached 104 mg per 100 cc. In 3 days the blood count had fallen to 22,400. The patient was discharged without treatment for leukemia, but returned 2 months later, again with lobar pneumonia. The white-cell count, which was 74,000 at the time he received sulfapyridine, was 49,000 10 days later. This was not a clear-cut response. Both changes in the white cell count may have been due to coincidental infection.

The effect of sulfapyridine was studied in Case 7 (H M H 39-1083), Case 8 (H M H 36-915)

*Cases 6 and 9 are reported through the courtesy of the Medical Clinic, Peter Bent Brigham Hospital, Boston.

and Case 9 (P B B H 112506), all of which were cases of chronic myelogenous leukemia. Cases 7 and 8 were followed closely during the periods in which they received sulfapyridine, but there was no change in total or differential white cell count that could be attributed to the drug. In Case 9, the patient was admitted with lobar pneumonia, and was given the drug orally in adequate dosage. No significant change was observed either in total or differential white-cell count.

Sulfapyridine produced palpable changes in the lymph nodes of all the cases of lymphatic leukemia. The extent of this reaction varied with the dosage of the drug; it consisted of swelling, noticeable within twelve to eighteen hours after the drug had been given, followed by a slow decrease in size to less than that prior to treatment. The most marked reaction of this type followed intravenous administration of the drug in Case 1. It is possible that the effect of x-ray therapy might be considerably increased if it were given during the period of local reaction in the nodes.

We have presented these cases as a preliminary report. It is suggested that further investigation may identify related compounds more effective than sulfapyridine in producing this type of reaction. Experimental studies directed to this phase of the problem are being carried out.

SUMMARY AND CONCLUSIONS

Three of 6 cases of lymphatic leukemia showed a rapid fall in lymphocytes when sulfapyridine was given. A fourth case showed a similar but not conclusive response. This reaction to the drug is apparent within twelve to eighteen hours after its administration, and appears even when its blood level is low. It is a transitory effect. In none of the cases was the fall in total white-cell count attributable to granulocytopenia.

In 3 cases of chronic myelogenous leukemia, no comparable response to sulfapyridine occurred.

These observations are interesting because recent reports on the effects of sulfapyridine on the hematopoietic system emphasize granulocytopenia. The reactions reported here appear to be different, and suggest a specific effect on the leukemic lymphocytic cell.

REFERENCES

1. Liss, V. J., Fisk, F., and Johnson, A. C. Chemotherapy of gonorrhea with M & B 693. *Lancet* 2:1160-1163, 1938.
2. John, F. D. Agranulocytosis following treatment with M & B 693. *Lancet* 2:1500, 1938.
3. Cox, R. V., and Perley, J. R. Agranulocytic angina following administration of M & B 693. *Lancet* 2:1412, 1938.
4. Barnett, H. L., Harrison, A. F., Perley, A. M., and Rihoff, M. B. The treatment of pneumococcal infections in infants and children with sulfapyridine. *J. M. A.* 112:518-522, 1939.
5. Hodges, H. L., Silver, W. C., Jr., Walker, E. M., Curry, M., and Shirley, R. C. The use of sulfapyridine in primary pneumococcal pneumonia and in pneumococcal pneumonia associated with measles. *J. Pediatr.* 14:417-426, 1939.
6. Dwyer, V. D., and H. L. H. M. Granulocytopenia in sulfapyridine therapy. *J. M. A.* 113:1012-1017, 1939.

THE USE OF OXYGEN IN DEMONSTRATING POSTERIOR HERNIATION OF INTERVERTEBRAL DISKS*

JAMES L. POPPEN, M.D.†

BOSTON

IT HAS been established beyond a doubt that posterior herniations of intervertebral disks form another important link in the chain of etiologic factors that may cause low-back and sciatic pain, and that they form one of the most favorable conditions in the lumbosacral spine for surgical treatment. In the past this condition went unverified many times even though perhaps suspected, because the surgeon hesitated to introduce Lipiodol into the subarachnoid space unless there was reasonable assurance that herniation was present so that the oil could be removed at the subsequent laminectomy.

The true nature of these pseudotumors has been recognized for many years, and they were at times referred to as enchondromas. Dandy¹ was one of the first to describe and designate the condition properly. To Mixter and Ayer,² Mixter and Barr,³ and Hampton and Robinson,⁴ however, belongs the credit for emphasizing the importance of recognizing the posterior protrusion of the degenerated portions of intervertebral disks in the lumbosacral region, as well as for verifying the presence of such a protrusion by the use of Lipiodol and the fluoroscope. As soon as their work had been published, neurosurgeons as well as bone and joint surgeons suspected that many patients who had responded poorly to measures used to relieve sciatic pain probably had posterior herniations of intervertebral disks. This proved to be true in many cases, and because of this, perhaps, the actual percentage of patients who had herniations as a cause of low-back pain with sciatic radiation was somewhat distorted, and for a time Lipiodol was used oftener than was necessary. Nevertheless it has been shown in many sections of this country that posterior herniations of intervertebral disks do play a dramatic role in the large group of etiologic factors capable of producing sciatica, a reasonable estimate being probably 2 to 3 per cent. The only figures that are available at present are those of the Mayo Clinic as given in the apparently astounding number of well over 500 verified herniations that have been successfully operated on; in reality these represent only 1.8 per cent of all patients they see with low-back pain. In the Lahey

Clinic the percentage has been 3 since the first patient with herniated disk was operated on in 1936.

Until recently Lipiodol has been the agent usually employed in verifying the presence of herniated disks. A few untoward effects were noted. This naturally created an interest in developing a technic that would visualize the presence of herniated disks by a medium that would be less irritating and at the same time would quickly be dissipated from the subarachnoid space. Lipiodol does not disappear from the subarachnoid space for many years and may stay indefinitely. Periodic fluoroscopic examinations have demonstrated that it usually moves freely in the space and that only in a few cases does it become encysted. In cases in which the latter occurs or in which the subjective symptoms become more marked following the injection of Lipiodol, the oil is certain to receive the blame for the entire symptomatology. It must be remembered that an intraspinal lesion was present before oil was injected, and that the pain may therefore be only a part of the original picture. It is logical to assume, however, that if an active, acute or chronic inflammatory change is present in the form of arachnoiditis or radiculitis, any irritating substance that remains in the spinal canal for years may produce denser adhesions, and Nature may attempt to wall off the foreign material and create a cystic arachnoiditis. For that reason, if an inflammatory condition is suspected, the use of Lipiodol should be avoided.

At the present time oxygen is used exclusively at the Lahey Clinic to demonstrate defects in the lumbosacral canal, and we consider it to be as efficient as Lipiodol in the visualization of posterior herniations of intervertebral disks. This statement would have been considered entirely too enthusiastic in our early experience with air, since the technic and lack of ability to interpret the spinogram failed to demonstrate accurately the presence of an intraspinal defect. However, by the continued co-operation of the radiologists, the importance of which cannot be overemphasized, a satisfactory routine has been instituted.

Following the pioneer work of Dandy, to whom, of course, belongs the credit for using air to visualize the intracranial and intraspinal fluid spaces, Coggeshall and von Storch,⁵ in Boston, and

*Department of Neurosurgery, Lahey Clinic.

†Neurosurgeon, Lahey Clinic.

Scott, Young and Chamberlain,⁶⁻⁸ in Philadelphia, were among the first to publish reports on the use of air in myelography.

It is true that the Lipiodol method is considerably easier for both the surgeon and the radiologist, since it takes only a relatively short time to



FIGURE 1

The patient is placed on the x-ray table with the side up in which the pain is severest. The head is elevated while 40 cc of fluid is allowed to escape from the spinal canal.

complete the introduction of Lipiodol and the fluoroscopy. Fluoroscopic examination is of no value in oxygen spinograms with the present x-ray equipment. The use of oxygen is much more

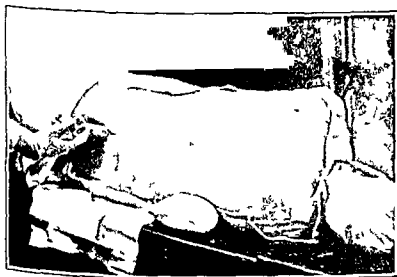


FIGURE 2

The table is then tilted to the Trendelenburg position, 30° angle, and the escaped fluid is replaced by 50 cc of oxygen.

time-consuming, since it is imperative that an accurate filling of the lower canal be made and that the wet films be examined before the patient is removed from the x-ray table. This, of course, is when most of the time is lost. If the roentgenograms are satisfactory, that is, if they demonstrate the deformity or show an entirely normal canal, nothing further has to be done. On the other

hand, at times there may be a suspicious defect, although not conclusive, and it is then necessary to take small spot stereoscopic films of the region in question.

The technic that is now used is as follows. The patients chosen for this procedure are those who have low back pain with or without sciatic radiation, in whom roentgenograms of the spine and sacroiliac regions do not show adequate cause for

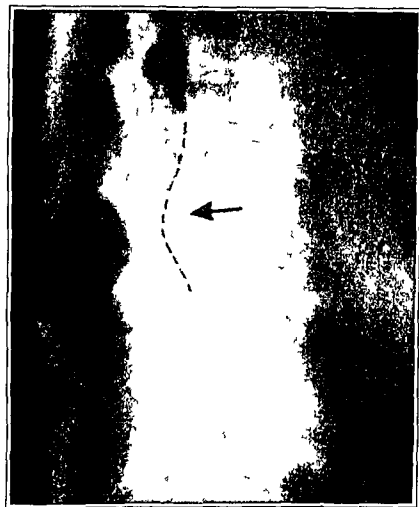


FIGURE 3

A sloping defect is demonstrated which separates the posterior longitudinal ligament from the superior margin of the fourth lumbar vertebra to the inferior margin of the fifth.

their discomfort and who have had sufficient investigation, including a neurologic examination and the elimination of foci of infection. The patient is given a large amount of premedication, usually including morphine and some form of barbiturate. He is then placed on a tilting table with head and shoulders higher than the rest of the body, in other words, Fowler's position, on the side opposite the pain. A spinal needle is inserted into the subarachnoid space between the fifth lumbar and first sacral spinous processes (Fig 1). Studies of the dynamics are carefully performed, and the first 2 or 3 cc of fluid is kept separate for determination of the total protein, after which 40 cc of fluid is allowed to escape or is aspirated with the syringe. The patient may complain slightly of a headache on withdrawal of the fluid

He is then tilted downward to a 30° angle (Fig. 2). A 50-cc. syringe filled with oxygen is attached to the needle, and the entire amount injected at one time, although not too rapidly. The patient usually says that the hip on the upper side feels numb immediately after the oxygen is introduced. A simple way of obtaining the oxygen is by attaching a sterile rubber tube to the oxygen outlet and allowing the oxygen to flow through this into the closed syringe. The pressure of the oxygen will slowly dislodge the piston until the

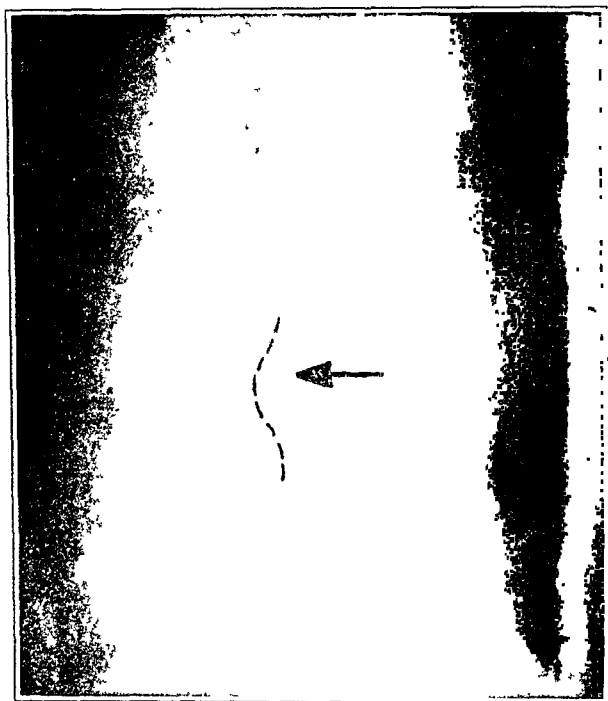


FIGURE 4.

This shows a sharply demarcated posterior protrusion, with the posterior longitudinal ligament separated only opposite the intervertebral space.

amount desired has entered the syringe. The needle is withdrawn with the syringe still attached. Lateral roentgenograms may be taken at this time, thus avoiding too much turning of the patient. The patient is then placed on his back, and the anteroposterior exposures are made.

It was at first thought necessary to take many oblique views to demonstrate defects in the oxygen column. However, we have found them of little value. In our experience, the stereoscopic anteroposterior and lateral views, if proper filling has taken place, demonstrate any defect that could be seen by other views. If the patient is allowed to remain in the Trendelenburg position for twelve to eighteen hours, little discomfort or headache will be noted.

Because of the lack of density, oxygen spinograms do not lend themselves to reproduction so well as Lipiodol spinograms. Nevertheless, with the stereoscopic view and proper interpretation, oxygen spinography is satisfactory and far superior in cases in which some question exists as to whether Lipiodol should be introduced. Such patients can have spinograms with oxygen taken without fear of untoward result.

Oxygen spinograms were made in 175 patients suspected of having herniated intervertebral disks. Of these, 150 were proved to have herniated disks by operation. In 5 of the latter it was necessary to inject Lipiodol as well as oxygen before the diagnosis could be made, this being due to faulty technic or to improper interpretation of the films at the time when we were inexperienced in the



FIGURE 5.

This represents a normal lumbosacral subarachnoid space filled with oxygen.

use of oxygen. In 25 cases the spinograms were interpreted to be negative, and for that reason the patients were not subjected to operation. How many of these will prove to have a herniated intervertebral disk at a later date is of course not known. It is only fair to say that the percentage of oxygen spinograms that were negative for herniation may be greater than that with Lipiodol, since no hesitancy is exercised in using oxygen in

patients whose histories and findings are not entirely typical of the condition. Lipiodol is still used if the herniation is suspected at a level higher than that of the twelfth thoracic vertebra, provided that subarachnoid block is not present; if a block is demonstrated, oxygen is used. It is conceivable that filling the entire spinal canal by the cisternal route, such as is done by a few neuro-

noid space around the nerve root, with only a very slight defect in the main air column. The lateral views are of no great value in demonstrating this type of lesion, since it may be completely covered with a layer of oxygen.

A posterior defect may often be seen in the air column, with an associated lipping of the posterior edges of the bodies of the vertebrae. However, the roentgenograms which show posterior lipping of all the lumbar vertebrae, with slight protrusions causing defects in the air column, certainly must not be considered similar to the single ones, since the subarachnoid space around



FIGURE 6.

In this film there is a sharply localized defect.

surgeons, may demonstrate the cervical, thoracic and upper lumbar canal satisfactorily. Interpretation of the spinograms is not difficult in most cases, but it may be exceedingly so. It behooves the roentgenologist and neurosurgeon to study the films stereoscopically, and when oxygen is used decision must often be reserved until the roentgenograms have thoroughly dried so as to avoid the possibility of overlooking a small lateral defect.

In the interpretation of the spinograms, considerable difficulty is first experienced in disregarding the many overlying outlines of bone. This is true to a lesser extent in the lateral stereoscopic views than in the anteroposterior views. Since the great majority of defects are found between the fourth and fifth lumbar and the fifth lumbar and first sacral vertebrae, considerable time should be taken in studying this region. The small lateral defects can usually be demonstrated in the anteroposterior view by lack of filling of the subarach-

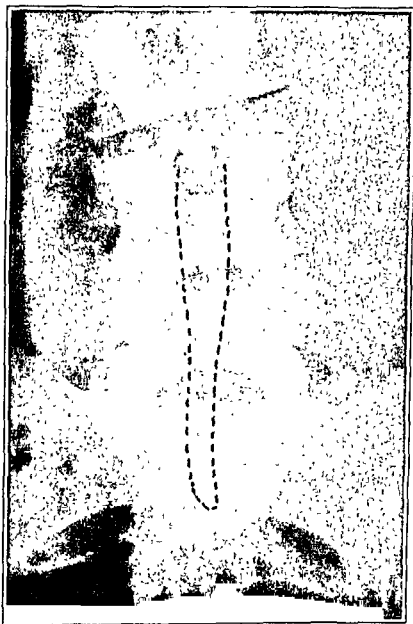


FIGURE 7.

This demonstrates a sloping lateral defect pushing the canal to one side rather than indenting it, as shown in Figure 6.

the nerve roots can be seen to fill normally in the former. These cases should be classified as posterior protrusions of intervertebral disks rather than as herniation or rupture. Laminectomy is not considered in this type.

There is, of course, considerable variation in the type of defect in the air column in different patients. The lateral view may show no defect, especially if the protrusion is small and laterally

placed, whereas it may show the longitudinal ligament separating from the immediate posterior surface of the fourth body near its upper end to the inferior margin of the fifth body below, causing a sloping protrusion (Fig. 3) or an acute defect sharply limited to the interspace (Fig. 4). Columns of oxygen do not lend themselves well to reproduction, and for that reason the anteroposterior views, when not seen stereoscopically, show only a faint outline (Fig. 5), which is a normal dural lumbosacral canal; however, a rather sharp defect may be seen in the lateral portion of the dural canal at the lumbosacral junction (Fig. 6). At times one can demonstrate a defect that seemingly displaces the dural canal away from the lesion rather than indenting it (Fig. 7).

SUMMARY

Oxygen spinograms on 175 patients suspected of having herniated intervertebral disks were thought to be positive, and later verified by operation, in 150. In 5 of these, Lipiodol was injected because the oxygen spinograms were found to be unsatisfactory because of faulty technic or of improper interpretation at the time when we were

inexperienced in the use of oxygen. In 25 cases the spinograms were interpreted to be negative, and the patients were not subjected to operation.

The advantages of oxygen over Lipiodol are obvious. The disadvantages are: there is increased temporary discomfort for the patient; re-examination is impossible at a later date unless the entire procedure is repeated; as a contrast medium, oxygen is relatively poor.

605 Commonwealth Avenue.

REFERENCES

1. Dandy, W. E.: Loose cartilage from intervertebral disk simulating tumor of the spinal cord. *Arch. Surg.* 19:660-672, 1929.
2. Mixter, W. J., and Ayer, J. B.: Herniation or rupture of intervertebral disc into the spinal canal: report of thirty-four cases. *New Eng. J. Med.* 213:385-393, 1935.
3. Mixter, W. J., and Barr, J. S.: Rupture of the intervertebral disc with involvement of the spinal canal. *New Eng. J. Med.* 211:210-215, 1934.
4. Hampton, A. O., and Robinson, J. M.: The roentgenographic demonstration of rupture of the intervertebral disc into the spinal canal after the injection of lipiodol. *Am. J. Roentgenol.* 36:782-803, 1936.
5. Coggeshall, H. C., and von Storch, T. J. C.: Diagnostic value of myelographic studies of the caudal dural sac. *Arch. Neurol. & Psychiat.* 31:611-613, 1934.
6. Scott, M., and Young, B. R.: Air myelography in the diagnosis of lesions of the spinal canal, with special reference to those of the nucleus pulposus and to the "sciatic syndrome." *Arch. Neurol. & Psychiat.* 38:1126, 1937.
7. Young, B. R., and Scott, M.: Air myelography: substitution of air for lipiodol in roentgen visualization of tumors and other structures in the spinal canal. *Am. J. Roentgenol.* 39:187-192, 1938.
8. Chamberlain, W. E. and Young, B. R.: The diagnosis of intervertebral disk protrusion by intraspinal injections of air: air myelography. *J. A. M. A.* 113:2022-2024, 1939.

REPORT ON MEDICAL PROGRESS

FIRST-AID TREATMENT FOR ASPHYXIA

CHARLES C. LUND, M.D.*

BOSTON

BECAUSE a physician is seldom present when asphyxial accidents occur, the contributions of the medical profession in this field are usually carried to the victims of accidents through an intermediary, a layman trained in first aid. Here the responsibility of the profession to the public is similar to that in connection with nursing technic—that is, a responsibility for research, education and standards of performance. Any new developments in knowledge or technic must be very carefully considered and tested because of the tremendous task of re-education involved. For the benefits of any new scientific discoveries used directly by the profession to be of value to the public, the education of the profession, and the education of the public to accept or demand the new services from the profession are essential. In first aid, however, there are three steps: education of the profession, education by the profession of

first-aid men to understand and accept the methods, and education of the public to accept or demand the new technics. Without enthusiastic promotion by physicians, progress in first aid is apt to be slow. Improvements in the technic of first aid for asphyxia have not been marked in the last ten years, but the diffusion to trained first-aid men of the knowledge of the gains of the previous twenty years has progressed very rapidly; consequently a large body of intelligent men in all walks of life now know what to do in cases of drowning and other types of asphyxia. Many of these have made a profession of first aid and rescue work, and are to be found largely among rescue crews of gas companies, attendants at public bathing beaches and teachers of first aid employed by such organizations as the American Red Cross. Because all members of the medical profession have not become familiar with the modern methods taught these men and have not had the practical experience in handling victims of drown-

*Assistant professor of surgery, Harvard Medical School; assistant visiting surgeon, Boston City Hospital.

ing and asphyxia, embarrassing situations occasionally arise. Above all, physicians must be very careful not to pronounce death prematurely in victims receiving artificial respiration, since nothing can hurt the profession more than to have a layman save a victim after a doctor has pronounced him dead—this has actually happened.

Victims of drowning or other types of asphyxia who show any sign of life must have immediate aid to survive. Place the victim in the prone position suitable for artificial respiration and then *give it*. No time must be wasted finding the best possible place, whatever reasonably good place can be reached in a few seconds must be used. The head must be turned to one side and must rest on the victim's hand, this keeps the mouth out of water or sand. If possible the body must lie head downward on a 20 or 30° slope, so that any fluid may easily run out of the bronchi and trachea. Then the prone pressure (Schafer) method of artificial respiration must be used. This procedure has displaced all other methods, for good physiological reasons,¹ except in the later stages of pregnancy or after an abdominal operation, when the Sylvester method is better.² The technic is described in all modern first aid manuals published in the United States and Great Britain.³ In addition to artificial respiration, every effort, short of stopping the attempt at resuscitation, must be made to keep the victim warm. Stimulants are of no use, and most of them are harmful—except, possibly, caffeine given in moderate dosage in travenously.

An advance in technic for certain cases was recently published by Drinker⁴ and by the Consolidated Edison Company of New York.⁵ This new technic, called "pole top resuscitation," was devised to reduce one type of preventable death, namely, that of the shocked linesman who receives artificial respiration too late because of the difficulty of getting him to the ground. The paper and the booklet give detailed instructions how to approach the unconscious man who is hanging by his safety belt and how to put him in proper position for artificial respiration astride the rescuer's safety belt. Then come the following instructions that are of interest to any student of artificial respiration because they show the necessity of adapting technic to special conditions in exceptional circumstances.

He shall then push the victim's head forward and apply pole top resuscitation by following these steps:

Encircling the man's waistline with his arms, placing one open hand on the abdomen and grasping the first hand with the fingers of the other to insure a firm grip.

Applying pressure upon the man's abdomen in an

inward and upward direction, then completely release pressure, to a time rhythm similar to that of normal breathing, which is approximately about four seconds a stroke.

The booklet contains a chart that shows the importance of speed in all rescue work so that artificial respiration may have a chance of success (Fig. 1). This chart is equally applicable to

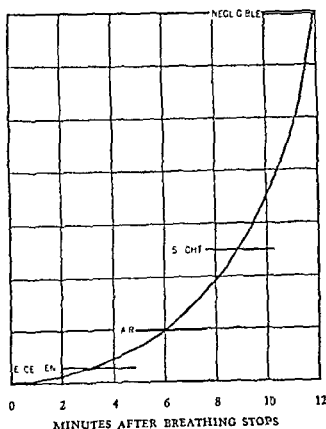


FIGURE 1 Cessation of Breathing and Resuscitation (Reproduced from Pole Top Resuscitation⁵ by permission of the publisher.)

It is assumed that a healthy adult stops breathing at 0. The chances of restoring respiration by appropriate measures are indicated by the curve.

drowning accidents. It should be remembered that the person who is removed from water and is not breathing continues to drown until artificial respiration starts. In all steps up to this, immediate and prompt action is absolutely essential. People have died after ceasing to breathe for two minutes, in spite of subsequent, continuous and presumably adequate artificial respiration. Conversely, nobody can live whose lungs have had no change of air for over twelve minutes.

Granted that the victim has a chance of survival at the start of artificial respiration, the procedure must be kept going for at least two hours unless good spontaneous respiration or positive signs of death have supervened.

INHALATORS

When asphyxia results from electric shock, drowning in water or solids, inhalation of a solid body, or breathing air of low oxygen content,—in sewers and under certain conditions in mines

—the problem is to get oxygen into the lungs. This can be done with artificial respiration in normal air about as rapidly as with any special oxygen mixture, even if the oxygen is immediately available. Asphyxiation with carbon monoxide is a different problem. A full consideration of all aspects of this problem will be found in the recent book by Drinker.⁶ With this type of asphyxia, artificial respiration with oxygen, as first suggested by Bernard⁷ in 1857, is better than artificial respiration with air. Better still is the administration of a mixture of oxygen and carbon dioxide, which was first recommended by Henderson and Haggard.⁸ Originally they suggested a mixture containing 90 per cent oxygen and 10 per cent carbon dioxide, but in 1922 they⁹ reduced the carbon dioxide content to 5 per cent for field use. Further experience showed that this mixture did not produce the optimum stimulation of respiration, and in 1929, following a study by Heller, Killiches and Drinker,¹⁰ a shift to 93 per cent oxygen and 7 per cent carbon dioxide was suggested. Following this, emergency crews using the new mixture reported a prompt decrease in the percentage of deaths in treated cases. This mixture has been standard ever since.

This gas mixture is given through a respirator held over the face by one man while another gives artificial respiration. It is important to keep administering the gas for one to two hours after spontaneous respiration has been established, and to be ready to readminister it at any time within the next twenty-four hours if normal respiration should become too shallow.

Several inhalators are on the market, and a few—the H-H, the B-K and the Davis—have been accepted by the Council on Physical Therapy of the American Medical Association. In principle they are like an old type of apparatus to give nitrous oxide anesthesia, being arranged to prevent rebreathing. It must be remembered, however, that in asphyxia due to carbon monoxide as well as in other types immediate artificial respiration is essential, and that there must be no delay while waiting for apparatus.

THE USE OF RESPIRATION APPARATUS

The idea of blowing air into the lungs and sucking it out again has always appealed to the inventive genius of the human race. Keith¹¹ gives a history of such devices up to 1909. Any contrivance that is to be successful in giving “suck-and-blow” artificial respiration must be safe and effective. One of the dangers is that of causing pulmonary collapse and atelectasis. The lungs will

stand very little pressure applied through the trachea. Any machine that blows in gas can potentially inflate the lungs to the bursting point with release of less than a thousandth part of the original pressure in the gas tank. Proper mechanical devices can probably eliminate most of this danger, but to date no such machine has eliminated all danger and at the same time provided a type of artificial respiration so safe, sure and foolproof as that applied manually by trained men. The old Pulmotor was so harmful that even in spite of the sale of thousands the company producing it failed and went out of business after a report by the Commission on Resuscitation from Carbon Monoxide Asphyxia¹² in 1923. Recently another “resuscitator” has come on the market and has been accepted by the Council on Physical Therapy of the American Medical Association.¹³ This one, the E and J Inhalator and Resuscitator, was accepted over the strenuous protest of Henderson¹⁴ who believes that the resuscitation part of this machine is just as dangerous as the Pulmotor, because mechanically it is very similar. He protested because he was afraid of two results from the use of the machine: first, that people would delay artificial respiration while waiting for the machine, and secondly, that it would be ineffective or harmful oftener than either manual or inhalation treatment. In its counterargument the council’s¹⁵ main contentions were as follows: that Coryllos’s¹⁶ work convinced the council that this apparatus was of life-saving value—the council quotes from a reference that is the same as one from which Henderson quotes as showing the device to be harmful; that artificial respiration plus an inhalator takes two trained men to operate, whereas the resuscitator can be managed by one; that the resuscitator is more practical to use on a pregnant woman or on a person with fractured ribs; that, “they [trained men] demonstrated completely their ability to use this apparatus to the complete satisfaction of the committee.” However, devices such as the Pulmotor or “resuscitators” are not recommended by large public-utility companies, any government bureau, or the American Red Cross. Mr. James L. Fieser,¹⁷ vice-chairman of the American Red Cross, has made the following statement:

We believe the prone-pressure method to be the best system of producing artificial respiration for our use, particularly because of its adaptability to the character of the people to whom our life-saving and first-aid instruction is given and because it is always ready for use by anyone instructed in its performance. For these reasons the purchase of mechanical resuscitation devices is not considered a proper expenditure of chapter funds.

MECHANICAL EXTERNAL-PRESSURE RESPIRATORS

Respirators, such as the Drinker, Emerson and others, or tilting tables may be used for continuous applications of artificial respiration for long periods of time. These are not first-aid appliances, but hospital equipment. In some cases of carbon monoxide poisoning, especially those complicated by drugs or alcohol, a very long period of artificial respiration and inhalation may be necessary, such patients should be transported to the nearest hospital that has a machine of this type.

ARTIFICIAL RESPIRATION DURING TRANSPORTATION

It is not generally realized that manual artificial respiration, with or without inhalation treatment, can be carried on in an ambulance.²⁸ In the past, just criticism has occasionally arisen because of the fact that patients undergoing artificial respiration lost their chances of recovery when ambulance crews took them to a hospital before artificial respiration had been given sufficient time to prove or disprove its utility. In cases that have to be moved, the treatment should be kept going in the ambulance, and the victim should be placed in a respirator or manual artificial respiration should be continued as soon as the hospital is reached. In such cases the necessary lapses in treatment must be as short as possible. For example, after stopping treatment to put the victim on a stretcher, treatment should be given for two or three minutes before picking up the stretcher. Again, treatment should be resumed after coming

down one flight of stairs and before starting another. Each interval of cessation of treatment should not be longer than thirty seconds.

319 Longwood Avenue

REFERENCES

- 1 Schafer E. V. Artificial respiration in man. *The Harvey Lectures* 1907-08. 266 pp. Philadelphia: J. B. Lippincott Co., 1909. Pp. 223-243.
- 2 Drinker C. K. *Instruction in the Application of Modern Methods of Resuscitation in Cases of Gas Poisoning, Electric Shock, Submersion (apparent drowning) and Suspended Respiration from Other Causes*. 15 pp. New York: Consolidated Edison Co. of New York, Inc. 1938.
- 3 *First Aid Manual*. 256 pp. Washington: American Red Cross. 1937.
- 4 Drinker C. K. Remarks on pole top resuscitation. 3 pp. Reprinted from the *Records of the Public Utilities Sessions*. 28th National Safety Congress and Exposition. National Safety Council. Atlantic City. October 16-20. 1939.
- 5 *Pole Top Resuscitation*. 10 pp. New York: Consolidated Edison Co. of New York, Inc. 1940.
- 6 Drinker C. K. *Carbon Monoxide Asphyxia*. 276 pp. New York and London: Oxford University Press. 1938.
- 7 Bernard C. *Leçons sur les effets des substances toxiques et médicamenteuses*. 488 pp. Paris: J. B. Baillière et Fils. 1857.
- 8 Henderson Y. and Haggard H. W. The elimination of carbon monoxide from the blood after a dangerous degree of asphyxiation and a therapy for accelerating the elimination. *J. Pharmacol. & Exper. Therap.* 16:11-20. 1920.
- 9 *Idem*. The treatment of carbon monoxide asphyxia by means of oxygen + CO₂ inhalation. *J. A. M. A.* 79:1137-1145. 1922.
- 10 Heller F., Killish W. and Drinker C. K. The evaluation of 5 and 7 per cent carbon dioxide mixtures as respiratory stimulants. *J. Indust. Hyg.* 11:293-300. 1929.
- 11 Keith A. Three Hunterian Lectures on the mechanism underlying the various methods of artificial respiration practiced since the foundation of the Royal Humane Society in 1774. *Lancet* 1:745-749. 825-828 and 895-899. 1909.
- 12 Final report of the Commission on Resuscitation from Carbon Monoxide Asphyxia: the treatment of carbon monoxide asphyxia. *J. Indust. Hyg.* 5:125-129. 1923.
- 13 Council on Physical Therapy. E & J Resuscitator and Inhalator acceptable. *J. A. M. A.* 112:1945. 1939.
- 14 Henderson Y. An open letter. *J. A. M. A.* 112:1946-1948. 1939.
- 15 Council on Physical Therapy. Reply to the open letter from Dr. Vandell Henderson. *J. A. M. A.* 112:1948. 1939.
- 16 Coryllos P. N. Mechanical resuscitation in advanced forms of asphyxia: clinical and experimental study in different methods of resuscitation. *Surg. Gynec. & Obst.* 66:698-727. 1938.
- 17 Freese I. L. personal communication.
- 18 *First Aid and Resuscitation in Gas Poisoning, Electric Shock and Drowning*. 16 pp. New York: Consolidated Edison Co. of New York, Inc. 1938.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 26501

PRESENTATION OF CASE

A seventy-year-old housewife entered the hospital complaining of substernal pain of five days' duration.

Three years before admission the patient came under observation in the Out Patient Department for diabetes mellitus. This was controlled satisfactorily with daily injections of 12 to 16 units of protamine insulin and an average caloric intake of 1367, made up of 104 gm. of carbohydrate, 69 gm. of protein and 75 gm. of fat. She carried on without incident until two years before admission, when she caught a cold and came to the Out Patient Department two weeks later complaining of asthma and evening dyspnea. It was found also that she had had a nonradiating, substernal oppression on exertion and swelling of her feet for a year or more. On examination the patient was able to lie flat without difficulty. The left border of the heart was 10.5 cm. from the midline, and the rhythm was regular. The sounds were rather distant; the aortic second sound was greater than the pulmonary second, and there was a systolic murmur at the base. The blood pressure was 200 systolic, 110 diastolic. Rales were heard at the lung bases posteriorly, and there was moderate pitting edema of the shins. With rest, and decreased fluid and salt intake, her condition improved, though the blood pressure always remained in the neighborhood of 205 systolic, 115 diastolic, and her ankles became slightly swollen at night.

Five days before admission marked the onset of a severe, nonradiating substernal pain that required medication by her physician. This was accompanied by numbness in both arms, anorexia and occasional vomiting. At the time of admission the patient stated that the pain was still present, though she seemed in no acute distress.

The past illnesses and family history were irrelevant.

On physical examination the patient was a pale, obese (174 pounds) woman lying flat in bed in no discomfort. There were bilateral cataracts, which obscured the fundi. The cardiac apex was palpated 13 cm. from the midline. The sounds were regu-

lar, but of poor quality, and a loud, grating, systolic murmur, heard best in the fourth interspace 6 cm. from the midline, was transmitted in all directions. The pulmonary second sound was louder than the aortic. The blood pressure was 120 systolic, 86 diastolic; only two weeks previously it had been 180 systolic, 110 diastolic. The peripheral arteries were palpable and tortuous; no pulsation could be felt in the dorsalis pedis arteries, but the feet were warm. The pulse was regular but thready. Bubbling rales were heard at the lung bases and as high up as the scapulas. There was right-flank tenderness. Heberden's nodes were present. There was no peripheral edema.

The temperature was 100.2°F., the pulse 102, and the respirations 25.

Examination of the urine showed a ++ test for albumin, the sugar reaction was yellow, and the sediment was loaded with white blood cells. Examination of the blood showed a red-cell count of 3,740,000 with a hemoglobin of 75 per cent, and a white-cell count of 22,300 with 79 per cent polymorphonuclears. The hematocrit reading was 39 per cent, and the corrected sedimentation rate 0.9 mm. per minute. The blood sugar was 600 mg. per 100 cc. The nonprotein nitrogen of the blood serum was 85 mg. per 100 cc., and the chlorides 92.6 milliequiv. per liter.

X-ray examination of the chest showed the position of the diaphragm to be high, and there was transverse enlargement of the heart, particularly in the region of the left ventricle. The aorta was markedly tortuous, and the pulmonary vessels slightly wider than usual.

Electrocardiographic recordings showed a rate of 100 with a regular rhythm. There was moderate left-axis deviation. T_1 was upright, T_2 biphasic and T_3 inverted. There was no change in ST_1 , ST_2 or ST_3 . R_4 was absent, Q_4 deep and ST_4 had a high take-off. T_4 was upright.

The patient was given 15 units of protamine insulin and 20 units of regular insulin daily, but her condition was precarious from the start and grew steadily worse. For the first four days the blood sugar remained around 500 mg. per 100 cc., but the sugar reaction in the urine varied from green to orange with 0 to + test for acetone. The nonprotein nitrogen of the blood serum rose steadily. For the next two days the blood sugar fell to 236 mg. per 100 cc., but the patient continued to vomit a brown, guaiac-positive fluid. Consequently she was given dextrose and saline by clysis, and dextrose and water by duodenal tube. The patient died on the eighth hospital day, at which time the blood sugar was 752 mg. per 100 cc. with a green sugar reaction in the urine. The

nonprotein nitrogen of the blood serum had risen to 145 mg. per 100 cc.

DIFFERENTIAL DIAGNOSIS

DR. PAUL D. WHITE: One of the important points of interest in this case is the common relation between diabetes mellitus and cardiovascular disease. Just this morning some of us have had the opportunity of listening to Dr. Paul Harrison, of Arabia. This sort of patient would not be met with in Arabia. Diabetes practically does not exist there, nor hypertension, nor some of the other conditions found in this case. There are thus certain advantages as well as disadvantages in living in Arabia.

This woman's substernal pain lasted five days. That is a long time. One would like to know, and there is a little more information later, whether the pain was continuous or came in waves, and whether it was paroxysmal. I might add that at the age of seventy, as Dr. Mallory has often pointed out, we should expect to make multiple diagnoses. Is it over fifty that you think one should make more than one diagnosis, Dr. Mallory?

DR. TRACY B. MALLORY: I think sixty is perhaps a safer dividing line.

DR. WHITE: We do not know how long she had had diabetes, nor can we dismiss it as mild, since she required insulin at this age.

One wonders whether the asthma was related to the cold, or whether some other factor such as cardiac weakness was behind it. We cannot tell with certainty from the available information. There is a fair story of angina pectoris.

Edema of the feet in a person as heavy as this patient may be due simply to a local circulatory fault with varicosities. Of course one has to think of weakness of the heart muscle, but the great majority of patients in the Out Patient Department here who come in with bilateral edema of the feet have no heart disease. Evidently this patient had no serious left or right ventricular failure.

One would like more description of the murmur. Was it louder in the pulmonic area? It might have been, as recorded here, either an unimportant physiologic pulmonary systolic murmur or it might have been the important murmur of aortic stenosis. However, the aortic second sound was apparently quite loud, a strong point against a marked degree of aortic stenosis.

With this blood-pressure reading, hypertension has to be added to the diagnoses of diabetes and cardiac enlargement. An astonishing number of persons with left ventricular weakness fail to show rales in the lung bases; they are much

more often found in infection. Of course the patient had had a cold. Rales are also often heard in cases of pulmonary embolism. There can be multiple pulmonary emboli with rales at the lung bases simulating congestive failure. Or they may mean atelectasis. However, here they should be heeded in view of the story of dyspnea and swelling of the feet and moderate pitting edema of the shins.

Up to this point I think we are justified in considering that the patient had diabetes, hypertensive heart disease with effort angina pectoris, probably on the basis of coronary disease, and possibly also some weakness of the heart muscle.

Then comes the story of the acute onset of the severe present illness. I judge that she must have been given morphine. Pain is usually severe if it spreads to both arms. There is no statement of one arm's being affected more than the other. This pain was more likely due to coronary involvement than to other trouble in the chest, especially since both arms were involved. The vomiting could have been produced by the medication. It is commonly so in cases that I have seen. Patients usually vomit because of the morphine rather than from the coronary thrombosis, although some persons will vomit when they have a cardiovascular attack of any sort. This pain was of unusually long duration. The story to date sounds like that of an acute coronary thrombosis, despite the unusually long-continued pain. We must think of other conditions, but none of them seem likely.

The cardiac apex was palpated 13 cm. from the midline. That is increased 3 cm. However, one may question this measurement. The systolic murmur described is an unusually loud one. The quality is striking.

DR. SEDGWICK MEAD: It was first described in the Out Patient Department, and at that time it was noted that there was a systolic murmur at the base, which was not striking. When the patient was admitted to the ward we assumed there had been an increase in intensity. It was widely transmitted and so loud as to give rise to the question of aortic stenosis.

DR. WHITE: Was there a thrill with it?

DR. MEAD: No.

DR. WHITE: It was in the fourth space, out toward the apex. That is an unusual site of maximum intensity for the murmur of aortic stenosis, but it may be widely heard and sometimes is better heard at the apex than at the base, although that is not the rule. If there had been a change and this murmur became so striking, one must think of the development of something else like a valve lesion, a rupture or injury, or a septal de-

fect resulting from myocardial infarction. These are quite rare but are on record. I have seen one or two that I think might have been such, but without autopsy. In these cases we may not be able to decide, following myocardial infarction, whether there is simply a dilated heart with mitral regurgitation or rupture of the septum, which would give a murmur something like a Roger murmur to the left of the sternum in the fourth interspace. The latter is a distinct possibility here, but it is very rare.

With the difficulty in feeling the foot arteries, one must think of intrinsic aortic abnormalities. Coarctation of the aorta would be unusual in an old person, although it has been reported at ninety. Dissecting aneurysm is a little more likely and might also explain the pain. Dissection of the aortic wall may block the pulse to the feet. However this patient's feet were warm, the pulse was regular but thready, and she was very ill at this time. There was no extreme tachypnea, perhaps helping to rule out intrinsic pulmonary disease or pulmonary embolism, although one may have a relatively slow respiratory rate with pulmonary embolism.

There was a higher leukocytosis than is ordinary for coronary thrombosis, although we see it infrequently as high as 20,000.

"The aorta was markedly tortuous." That is what we should expect. It was apparently not wide, and the diagnosis of dissecting aortic aneurysm is not supported. This week Dr. Schatzki pointed out to us very interesting comparative x-ray films of patients before and after the development of dissecting aortic aneurysms; usually there is a clear indication of such a lesion by x-ray.

We might have suspected with such a large heart and hypertension of long standing that the T waves in Lead I would be inverted rather than upright, and that T₃ would be upright rather than inverted. As a matter of fact, this record does not show left-axis deviation.

DR. MEAD: This description is from an electrocardiographic examination that I made in the Emergency Ward and was not apparent in the next few tracings taken, but this is substantially what was observed at that time, and I was especially struck by the high ST segment in Lead 4.

DR. WHITE: There are two records here, and they are rather different. What is the time relation?

DR. MEAD: Two or three days apart.

DR. WHITE: These are very puzzling records but support the probability of coronary involvement, especially because of the absent R waves and high ST segments in Lead 4. The tracing

looks like one of a mixed type, perhaps due to an infarction in more than one spot or else very extensive.

The course here illustrates the difficulty of treating an old patient who has both diabetes mellitus and a severe cardiovascular lesion. One condition reacts unfavorably on the other and tends to retard or to prevent the recovery. We have fairly clear evidence here of cardiac enlargement due mostly to hypertension with coronary disease and diabetes. The difficult questions concern chiefly the cause of the pain of five days' duration, the unusual murmur that was heard on the second occasion, and the electrocardiographic abnormalities. I think we should expect to find coronary thrombosis, probably an old lesion, in addition to a new one with myocardial infarction. I should hesitate to place the infarct exactly, but it may have involved both the anterior apical portion of the left ventricle and the septum, and I shall take a chance on the possibility of there having been a perforation of the septum secondary to such a lesion but shall not rule out entirely the possibility of aortic stenosis that had not been evident previously, or at least had not been well enough described for diagnosis. Once in a while myocardial infarction involves the papillary muscle, which allows the rapid development of mitral regurgitation of high degree with a sudden appearance of a loud systolic murmur that one would expect to hear maximally at the apex. We have to consider that as a possibility. Finally, simply acute left ventricular dilatation secondary to coronary thrombosis can produce a fresh mitral systolic murmur. I should put as least likely a dissecting aneurysm of the aorta.

CLINICAL DIAGNOSES

Uremia.

Chronic vascular nephritis.

Diabetes mellitus.

Arteriosclerosis.

Myocardial infarction?

DR. WHITE'S DIAGNOSES

Hypertensive, coronary heart disease, with acute coronary thrombosis and large or multiple myocardial infarction involving the anterior apical portion of the left ventricle and probably the septum.

Acute perforation of the interventricular septum secondary to infarction, or acute relative mitral insufficiency secondary to involvement of the papillary muscles or simply to left ventricular dilatation.

Aortic stenosis?

Diabetes mellitus.

ANATOMICAL DIAGNOSES

Coronary thrombosis, left descending.
 Myocardial infarction.
 Cardiac dilatation, left ventricle.
 Pulmonary congestion, slight.
 Arteriosclerosis, marked: aortic, coronary and cerebral.
 Obesity.
 Hyalinization of islets of Langerhans (diabetes mellitus).
 Cerebral atrophy, slight.
 Gastritis.
 Leiomyoma uteri.
 Melanosis coli.
 Endometrial polyp.

PATHOLOGICAL DISCUSSION

DR. MALLORY: The autopsy showed an enlarged heart, weighing just over 400 gm. The coronary arteries showed extensive atheroma, and there was a point of complete occlusion due to a fairly recent thrombus in the descending branch of the left coronary artery. This had resulted in a large area of infarction at the apex of the left ventricle. The ventricle appeared diffusely dilated and particularly so at its apex, a condition that, if more marked, might have led us to talk about cardiac aneurysm. The myocardial wall at the apex was soft, discolored and thinned to 5 mm., whereas at the base of the heart it measured 18 mm. and was clearly hypertrophied. Microscopic sections through the area of infarction showed complete necrosis of the muscle cells, and the end of a polymorphonuclear reaction with leukocytes that were almost all necrotic, but as yet little in-wandering of mononuclear cells. The findings all seem consistent with a history pointing to infarction of a little less than two weeks' duration. The kidneys were of the ordinary hypertensive type. The pancreas on microscopic examination showed hyalinized islets of Langerhans, which we always hope to find in diabetes but frequently do not.

I neglected to speak of the aortic valve. Evidently that was examined with considerable care, I imagine at the urging of the clinician. We finally found very slight interadherence of two of the cusps, but the diagnosis of aortic stenosis was not made.

DR. WHITE: Was the papillary muscle involved?

DR. MALLORY: No, and the interventricular septum was only slightly so.

DR. WHITE: Probably the murmur was the result of dilatation of the heart, resulting from the infarct, which thus secondarily caused mitral regurgitation, even though the reported location of the maximal murmur was unusual.

DR. MALLORY: It hardly seems as if the anatomical findings in the aortic valve explained the murmur, although one cannot say it was absolutely normal.

CASE 26502

PRESENTATION OF CASE

A sixty-three-year-old blacksmith entered the hospital complaining of pain in the left chest.

Five months before admission the patient began to suffer from sharply localized pain and tenderness in the region of the third left rib close to the sternum, which radiated to the left shoulder blade. The pain was aggravated by deep breathing and coughing and was accompanied by a generalized weakness. It was constantly present as a dull ache and sometimes became severe. In addition he noticed "muscle pains" in both legs, which varied in location and intensity. For some years he had been examined every spring by his physician, and four months prior to entry albumin was found in his urine. Thereupon he consulted two other physicians, and all three made a diagnosis of Bright's disease. Three months before admission for a period of several weeks he had felt nauseated and frequently vomited after meals. Six weeks before admission a constant severe pain developed in the right subcostal region. It was aggravated by deep respiration, coughing, bending over and damp weather, compelled him to sleep on his right side or back, and often awakened him at night. A nocturia of three times a night developed. He had lost 50 pounds since the onset of his symptoms and for the past two months had had constipation, which required saline laxatives for relief. For the past month he had often felt "shivery" and needed more clothing for warmth. Three days before admission he vomited without nausea.

The patient had had arthritis at thirty-five. The family history was irrelevant.

On physical examination the patient was pale, appeared tired and showed evidence of weight loss. The breath had a uriferous odor. The mucous membranes were pale, and the scleras slightly icteric. Numerous soft, painless, freely movable, discrete tumors measuring up to 3 cm. in diameter were present over the entire body and especially over the chest and abdomen. These were consistent with multiple subcutaneous lipomas. Over the third left rib 4 cm. from the midline there was a sharply defined, depressed, 3-cm. area of tenderness. Palpation of this area revealed mobility and crepitation of the underlying rib, and, on auscultation, crepitus could be heard on inspira-

tion. There was pain on pressure over the lower fourth and fifth ribs anteriorly. The heart was slightly enlarged to percussion, and a systolic murmur was heard over the entire precordium and transmitted into the axilla; the blood pressure was 140 systolic, 70 diastolic. The abdomen was negative except for slight tenderness over the left side. There was a left hydrocele. Rectal examination was negative. The fundi were negative, except for slight tortuosity of the vessels. Examination of the nervous system was negative.

The temperature was 100°F., the pulse 90 and respirations 20.

Examination of the urine showed a ++++ reaction for albumin, with an Esbach quantitative albumin of 8.0 gm. per liter. There were numerous granular and a few cellular casts and 10 to 15 white blood cells per high-power field. Bence-Jones protein was never demonstrated, and cultures were negative. Examination of the blood showed a red-cell count of 2,000,000 with a hemoglobin of 50 per cent, and white-cell count of 7800 with 73 per cent polymorphonuclears, 15 per cent lymphocytes, 1 per cent eosinophils and no basophils. The red cells showed a marked variation in size and shape. An occasional plasma cell was reported in the blood smear. The nonprotein nitrogen of the blood serum was 115 mg. per 100 cc., the proteins 6.7 gm., the calcium 10.9 mg., the phosphorus 10.5 mg. and the phosphatase 3.3 units. A blood Hinton test was negative. Examination of the stools was negative.

X-ray examination of the skull showed three or four small areas of decreased density. There was marked destruction, with pathologic fracture, of the seventh dorsal vertebra. An area of destruction involved the ninth rib on the right, with increase in the size of the rib in the area of destruction. An area of destruction also involved the vertebral end of the ninth rib on the left side, with increase in the size of the rib in the area of destruction. There was localized new-bone formation about the articulations of the right fourth and fifth lumbar vertebrae. The femurs showed a number of minute areas of rarefaction just above the condyles, and the arteries of the leg showed advanced calcification. X-ray examination of the chest showed a soft-tissue thickening of the anterior extremity of the third left rib, but the underlying bone appeared normal. There was a sharply defined area of rarefaction in the lateral extremity of the left clavicle, and also an indefinite area of rarefaction in the mid-shaft of the right clavicle. The aorta showed a marked degree of tortuosity, and there was a suggestion of a mass at the left hilum. The peripheral portions of the lung fields were clear.

An intravenous pyelogram showed the kidneys to be normal in size, shape and position. Films taken up to forty minutes after injection of the dye showed no excretion on either side.

A gastrointestinal series at another hospital showed a normal esophagus, stomach and small intestine.

Eight days after admission the blood chlorides were 117 milliequiv. per liter, and the carbon dioxide combining power 11.1 milliequiv., and the nonprotein nitrogen had risen to 170 mg. per 100 cc. The patient failed rapidly and died on the eleventh hospital day.

DIFFERENTIAL DIAGNOSIS

DR. JAMES R. LINGLEY: These shadows in the skull are rather indefinite, but I think that there are a few small areas of rarefaction, two in the frontal region and one in the temporal. The most obvious lesion demonstrated on the films is the destroyed vertebra. The width of the body is markedly reduced. There is a definite pathologic fracture without any new-bone formation, and the intervertebral spaces above and below are preserved. The ninth rib shows some expansion near its articulation to the spine, as described, and there is also destruction of the transverse process of the ninth vertebra. Both femurs show very minute areas of rarefaction just above the condyles. These may be pathologic but could be due to atrophy. It would be unusual for atrophy, however, since the rest of the bones appear normal.

DR. ALFRED KRANES: Does the rest of the skeleton appear normal?

DR. LINGLEY: Yes. The chest shows a mass superimposed on the left hilum and arch of the aorta. In the lateral view it is not well visualized, but it probably lies posterior to the root of the lung and therefore represents a paravertebral mass rather than one due to lymph nodes at the hilum.

DR. KRANES: Then you do not believe it is in the lung?

DR. LINGLEY: I doubt it because the lungs are clear in the lateral view. I believe they are normal.

DR. KRANES: After reading this record we can be reasonably sure that this patient suffered from two conditions: a fairly advanced degree of renal insufficiency, and a malignant neoplasm of some type. Our problem seems equally clear cut, namely, to determine whether these two processes were independent of each other or related, and in addition to discuss the nature of the renal and skeletal lesions. And because Dr. Mallory has asked us to be brief, I shall confine my discussion only to a consideration of the more relevant possibilities and omit those that seem more remote.

We first have to consider whether the kidney

disease was independent of the skeletal disease, and if we assume that it is, we have to make a diagnosis of some sort of primary nephritis. It seems to me that the evidence in favor of such a diagnosis is very meager. We are fortunate in being told that this patient had been repeatedly examined by his physician, and at no time before his present illness were abnormalities of the urine demonstrated. I assume that the urine was examined, and it was not until four months before admission that albumin was found. It therefore seems unlikely that the patient had any pre-existing renal disease. Furthermore, the renal process did not behave like any of the chronic renal diseases, such as chronic glomerulonephritis, vascular nephritis and pyelonephritis. There is no hypertension, no evidence of cardiac enlargement by x-ray, although the physical examination showed the heart to be a little large, and no arterial changes except in the large vessels of the leg. Consequently I think any primary renal disease is improbable. Furthermore, one would like to cover the whole picture with one diagnosis if one could. So I shall go on and assume that both the renal and skeletal lesions were part and parcel of the same disease.

We then have to consider what types of malignant neoplasm will cause renal insufficiency. There are two ways in which cancer can cause renal insufficiency. One is by destruction of the renal parenchyma, and the other by obstruction of the urinary tract, either the urethra or both ureters. So far as the destruction of the renal parenchyma goes, I think it is highly improbable that any cancer would do that. A hypernephroma for example is almost always unilateral, and it would be unique for a hypernephroma or primary renal-cell carcinoma to destroy enough renal tissue to produce uremia. The same would be true of metastatic lesions to the kidney.

We come then to the possibility of obstruction to the urinary tract by cancer. In the male the two most frequent lesions producing urinary obstruction are carcinoma of the prostate and carcinoma of the lower gastrointestinal tract invading the pelvis and obstructing both ureters. So far as the prostate goes, one must admit the possibility of a small lesion in the prostate, not clinically obvious, which could produce this clinical picture. I think, however, that if it were extensive enough to produce urinary obstruction one would be able to feel something more than was felt by rectum in this patient. The same I think holds true for cancer of the gastrointestinal tract with pelvic metastases: one should be able to find some evidence of pelvic metastases by rectal examination.

Furthermore, I think the urinary picture is not that of urinary obstruction. If that were the case one would expect a decrease in urinary output, whereas this patient developed a polyuria. Nor is the urinalysis what one would expect with an obstructive lesion somewhere in the genitourinary tract. Eight grams per liter is a lot of albumin, and one ordinarily does not expect that amount of albuminuria with any obstructive lesion.

There is one disease that does explain this picture, and that is multiple myeloma. Whenever one is confronted with a disease with widespread involvement of the skeleton and also renal insufficiency of an unusual type, as I think we have here, one should always first consider multiple myeloma, the renal lesion, as you know, being due to deposits of Bence-Jones protein in the tubules. On the whole I think that is the best diagnosis I can make. In this particular case it may seem unwise to make that diagnosis in the absence of any confirmatory laboratory evidence. One would expect in repeated search that Bence-Jones protein might be found, but there are a considerable number of cases in which no Bence-Jones protein can be demonstrated. Nor does the normal serum protein exclude it. It is elevated in only half the cases. The fact that an occasional plasma cell was found in the blood does not mean much because that might be found in any blood.

There is one other disease that must be considered. Whenever we are confronted with the combination of skeletal and renal lesions, the question of hyperparathyroidism must be raised. But I think the evidence against it is too great in this case. The x-ray pictures show localized areas of destruction with intervening normal skeleton. One would not expect such localized lesions in hyperparathyroidism. Furthermore, the type of renal insufficiency here is not what one would expect with hyperparathyroidism in which the renal failure is due to one of two causes, either bilateral stones, of which there is no evidence, or calcification of the renal tubules, which, if it were extensive enough to cause such marked renal failure, might be expected to show by x-ray. So far as the chemical constituents of the blood are concerned, the pattern may have been masked a great deal by the renal insufficiency. A patient with hyperparathyroidism may have a low serum phosphorus, but when renal failure develops it rises. Similarly one may ask if a calcium of 10.9 mg. in a patient with marked renal failure does not actually represent an elevation of serum calcium, because ordinarily the calcium goes down in uremia. Considering all these possibilities I shall

make a diagnosis of multiple myeloma, with renal insufficiency due to myeloma kidneys.

DR. BERNARD JACOBSON: How does Dr. Kranes conceive of Bence-Jones kidneys without Bence-Jones protein in the urine?

DR. KRANES: I think that in some of the cases we have seen here Bence-Jones protein was not demonstrated in the urine, but the kidneys did show deposits in the tubules at autopsy.

DR. JACOBSON: Of the cases of myeloma about half died finally in uremia, and of some 8 or 9 cases that have died of uremia under our own eyes, all have had Bence-Jones protein in the urine during life. I agree with Dr. Kranes that the occasional plasma cell in the blood is normal.

DR. JOHN W. ZELLER: Is not amyloid disease of the kidney present in myeloma?

DR. TRACY B. MALLORY: Certainly not usually. It may be.

DR. LINGLEY: The minute areas of rarefaction in the lower femoral shafts interest me very much. Dr. Jacobson and I have been reviewing the cases of myeloma observed here during the last few years, and we think that, in some cases, these minute areas of destruction are one of the earliest roentgenological signs. They are extremely small and punctate, and unfortunately they usually cannot be differentiated from atrophy. In this case there is one small, oval area of rarefaction in the left clavicle that is more characteristic.

CLINICAL DIAGNOSES

Multiple myeloma.
Chronic nephritis.

DR. KRANES'S DIAGNOSES

Multiple myeloma.
Myeloma kidneys.

ANATOMICAL DIAGNOSES

Multiple myeloma.
Pathologic fractures of the third left rib and seventh dorsal vertebra.
Myeloma kidney.
Acute pyelonephritis.
Hypertrophy of the heart.

PATHOLOGICAL DISCUSSION

DR. MALLORY: At post-mortem examination the

most obvious lesions were in the skeletal system. The sixth, seventh and ninth ribs on the right and the third and fourth ribs on the left showed localized tumors. These for the most part lay within the marrow cavity and had expanded and thinned the cortex. In one place the tumor had produced a pathologic fracture, and in another it had broken through to form a mass 2.5 by 3 cm., which entirely surrounded the rib. The bodies of two vertebrae were entirely filled with tumor, one of them, the seventh dorsal, showing a compression fracture. From the margins of this vertebra two large paravertebral masses of tumor projected to either side of the spine. As is usual with myeloma no visceral metastases were found.

The other point of interest was, of course, the status of the kidneys. They were of normal size, weighing 350 gm., but the cortices were narrowed to 3 or 4 mm. The capsules stripped readily, revealing smooth surfaces mottled with irregular pinkish-gray patches. The cut surfaces showed similar mottling, and the gross appearances were thought to be suggestive of pyelonephritis, though there was no dilatation of the pelves or injection of their mucosa. The microscopic sections are not easy to interpret. There is evidence of considerable arteriolar sclerosis and of patchy atrophy of the cortex. There are a few small acute abscesses. The unusual feature is the abundance of dense hyaline casts in all parts of the tubule system. These might be interpreted either as the "colloid casts" of chronic pyelonephritis or as the coagula of Bence-Jones protein that plug the renal tubules in so many cases of myeloma. There is unfortunately no specific method of differentiation. Two points incline me to the second hypothesis; first, the casts are diffusely scattered throughout the tubule system rather than being concentrated in focal areas and, secondly, some of the casts are surrounded by foreign-body giant cells. This giant-cell reaction is very frequent in the myeloma kidney, whereas I cannot remember to have observed it in pyelonephritis. I am therefore going to side with Dr. Kranes against Dr. Jacobson. I should not be surprised, however, to find that other pathologists might disagree with my interpretation. Certainly in view of the scattered small acute abscesses we must admit some degree of terminal pyelonephritis as well.

The New England Journal of Medicine

Formerly the
Boston Medical and Surgical Journal
Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE
ON PUBLICATIONS

Official Organ of
THE MASSACHUSETTS MEDICAL SOCIETY
THE NEW HAMPSHIRE MEDICAL SOCIETY
THE VERMONT STATE MEDICAL SOCIETY

EDITORIAL BOARD

Joseph Garland M D	John P. Sutherland M D
William B. Breed M D	Stephen Ruthmore, M D
George R. Minot M D	Henry R. Viets M D
Frank H. Lahey M D	Robert M. Green M D
Shields Warren M D	Charles C. Lund M D
George L. Tobey Jr., M D	John F. Fulton M D
C. Guy Lane M D	A. Warren Stearns M D
William A. Rogers M D	Dwight O. Hara, M D

ASSOCIATE EDITORS

Thomas H. Lehman, M D	Donald Munro M D
Henry Jackson, Jr., M D	

Walter P. Bowers M D EDITOR EMERITUS
Robert N. Nye M D, MANAGING EDITOR
Clara D. Davies, ASSISTANT EDITOR

SUBSCRIPTION TERMS \$6.00 per year in advance, postage paid, for the
United States; Canada \$7.04 per year, \$8.52 per year for all foreign coun-
tries belonging to the Postal Union

MATERIAL for early publication should be received not later than noon
on Saturday

The Journal does not hold itself responsible for statements made by any
contributor

COMMUNICATIONS should be addressed to the *New England Journal of
Medicine*, 8 Fenway Boston, Massachusetts

TRUETA'S TREATMENT OF COMPOUND FRACTURES

Now that our country is mobilizing in prepara-
tion for all eventualities, including war, it behooves
the medical profession to be prepared technically
as well as spiritually for any contingency. A great
contribution to military surgery has come out of
the recent Spanish War, the major lessons of which
have been covered in a small book by Trueta,¹ of
Barcelona.

During World War I, surgeons became antiseptic
nihilists, and long before the war was over
the principle of thorough débridement for traumatic
injury to the body was well established. When the
Spanish War broke out, the surgeons began at the point
where they had left off. In the

previous war the most unsatisfactory surgical procedure
was the treatment of compound fractures. As a rule,
the extremities were kept in some form of traction
apparatus, and the wounds were left open after being
thoroughly débrided and were then dressed frequently,
with or without irrigations consisting of a neutral sodium
hypochlorite (Carrel-Dakin) solution.

A few exceptions to this care of compound fractures
occurred, principally one adopted by Rutherford Mor-
rison, of Newcastle, England. After débridement, Mor-
rison introduced "BIP" (bismuth iodoform paste) into
the wound, closed the wound loosely, and then put the
extremity in some form of immobilization apparatus,—
often plaster,—changing the dressings infrequently. Un-
fortunately this method did not receive universal ap-
plication, although in Morrison's hands the results were
satisfactory. A few surgeons, however,—notably Orr and
Baer in this country,—continued the procedure of im-
mobilization as a primary requisite for the proper treat-
ment of fractures of the extremities.

Gamgee as early as 1853 advocated the fixation and
infrequent dressing of wounds complicated by fractures.
Curiously, when Lister introduced antiseptics, a good
deal of this idea was lost and, indeed, did not reappear
in force and well supported by data until the Spanish
surgeons proved the greater efficacy of the immobiliza-
tion method. Perhaps our Spanish colleagues found them-
selves without fixation apparatus other than plaster of
Paris, or perhaps immediate débridement and complete
immobilization of all compound fractures seemed to be
the wisest method of procedure in bombed cities, where,
incidentally, the wounds were probably less seriously
contaminated than those seen by most military surgeons
in World War I. Whatever the impetus to this method
of therapy, it must now be accepted as vastly superior
to any as yet practiced by the military surgeon.

Trueta's monograph reports 1073 cases of com-
pound fracture of the limbs, most of them war wounds.
The 976 good or satisfactory results, with 6 fatalities,
are better by far than anything previously accomplished.
He gives a complete re-

view of the method used by the Spanish surgeons. In brief, the technic recommended for the immediate treatment of war fractures is as follows: immediate careful débridement of the wound, which must consist in excision of the skin edges and in the removal of all contused and damaged tissue, displaced or completely denuded bony fragments, and foreign bodies; complete immobilization of the limb in plaster of Paris, without the use of windows or bridges over the wounded area; injection of tetanus antitoxin; drainage, depending on the seriousness of the damage and the time since the injury; the skin should be left open, or if closed, the sutures must be few and allowance must be made for the discharge of material under the cast.

Of course the success of this therapy lies in early application. Obviously under the conditions of an air-raid where the patient is seen within an hour, the wound does very well; but the longer the interval between the injury and surgical attention, the less frequently this treatment can be followed. Trueta makes the statement that when the infection is gross and the cellulitis widespread, immediate surgery and immobilization in a closed cast cannot be resorted to. His usual technic, however, may somewhat alter the plans of the medical department of an army; for if such fractures are best treated by immediate immobilization, surgical teams should be far nearer the scene of bombing than ever before. Once a patient is in a plaster cast he is easily and simply transported.

In speaking of the value of immobilization of such compound fractures, Trueta emphasizes that rest allows the formation of local venous and capillary thrombi, thus preventing the spread of infection, and the formation of new capillaries, thus hastening healing. In fact this method is a criticism of the conscientious surgeon who, meaning well, dresses wounds so frequently that they cannot heal.

In speaking of the discharge from the wound that necessarily occurs beneath the plaster, Trueta lists the bad odor as the chief deterrent. This indeed was so great in the hot weather that casts had to be changed earlier than the surgeons desired. As a rule the first cast is changed in ten or

fifteen days, the second is left on for twenty or thirty days and the third is left on until healing is complete—in many cases for more than two months.

American observers² have confirmed the results of the Spanish surgeons, and there can be little doubt that the method henceforth should have the widest application. All surgeons contemplating military service should be familiar with this advance in the treatment of compound fractures.

REFERENCES

1. Trueta, J.: *Treatment of War Wounds and Fractures with Special Reference to the Closed Method as Used in the War in Spain*. 146 pp. New York: Paul B. Hoeber, Inc., 1940.
2. Eloesser, L.: *Treatment of compound fractures in war: reports of practical experience in the Spanish Civil War*. *J. A. M. A.* 115:1848-1852, 1940

MEDICAL EPONYM

FLAJANI'S DISEASE

The classic Italian description of toxic goiter is that of Giuseppe Flajani (1741-1808). The following translated extract is taken from an observation entitled "*Sopra un tumor freddo nell' anterior parte del collo detto broncocele*" [Regarding a cold tumor in the anterior part of the neck, called a bronchocele] in his book, *Collezione d'osservazioni e riflessioni di chirurgia* (*Collected Surgical Observations and Reflections*) (Rome, 1798-1803: Vol. III, p. 271).

There suddenly appeared in the anterior part of the neck of one Giovanni Spagnolo a tumor that in the course of four months grew to a considerable size so that it occupied the anterior and lateral aspects of the neck. He was under the care of his physician during a period of seven months, not so much because of the swelling as on account of the difficulty in breathing, continuous dyspnea and marked palpitation in the region of his heart. In the attempt to lessen these symptoms, the man had been obliged to abandon his occupation as a painter and to lead a life of idleness, thinking to avert an incurable organic condition.

Giovanni being then twenty-two years of age and being persuaded of the seriousness of his malady, requested some remedy by which the tumor might be lessened in size or by which its growth might at least be impeded, since it seemed that its pressure on the subjacent parts was gradually causing more difficulty in breathing and speaking. This was the story that the physician-in-charge gave me when I was called to see the patient. On inspection, the tumor seemed to be of considerable size and was apparently divided into two parts by a sort of central cleft. Externally the color was normal except for the veins, which were swollen as if varicose. There was no tenderness to touch, although pressure with the fingers caused difficulty in breathing. He was exhausted and emaciated, possibly because of frequent bleedings, to which he had been obliged to resort at least once a month.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS
AND GYNECOLOGY*

RAYMOND S. TITUS, M.D., *Secretary*
330 Dartmouth Street
Boston

DIABETES DEVELOPING DURING PREGNANCY
COMPLICATED BY HYDRAMNIOS

Mrs C., a thirty two year-old primipara, was first seen on July 3, 1939, when approximately thirty six weeks pregnant. She was referred by her family physician after a borderline diabetes had been discovered in the thirtieth week of pregnancy. This condition was being followed by a specialist in diabetes and was controlled by small doses of insulin.

The family history was noncontributory. The patient had an appendectomy at the age of nine, and a tonsillectomy at twenty. She also had had measles and chicken pox. Catamenia began at four teen, were regular with a twenty-eight-day cycle and lasted five days without discomfort. The last period began at the end of October, 1938, making the expected date of confinement early in August.

Physical examination revealed a well developed and well nourished woman. The weight was 133 pounds, a gain of 23 pounds over her normal weight. The heart was not enlarged, there were no murmurs. The lungs were clear and resonant, there were no rales. The blood pressure was 112 systolic, 70 diastolic. Abdominal examination revealed a fundus which was 29 cm. above the symphysis, the vertex was at the pelvic brim. The fetal heart was heard. Vaginal examination revealed an almost flat cervix, which was dilated to admit one finger. It was believed that labor would occur in about two weeks.

The patient was seen again by the obstetrician on July 6 and July 11. At neither of these visits was there any evidence of edema or elevation of the blood pressure. Blood prolan tests were normal.

On July 16 a vaginal examination revealed that the cervix was favorable for induction, the membranes were ruptured artificially, with the escape of a large amount of fluid. Labor started immediately, and in eight hours the patient was delivered by a simple forceps operation of a male child weighing 9 pounds, 3 ounces. The baby was in good condition.

The mother made an uneventful convalescence.

A series of selected case histories by members of the section will be read weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

she did not nurse. When seen in the office on August 28, the weight was 111 pounds and she seemed very well.

Comment This is a case of diabetes that was first recognized during pregnancy. The diabetes was very mild and was easily regulated with small doses of insulin. Labor was induced three weeks early because of definite hydramnios, which is characteristic of diabetic patients, and also to avoid intrauterine death. The size of the child, 9 pounds, 3 ounces, three weeks before full gestation is another characteristic of infants born of diabetic mothers.

MEDICAL POSTGRADUATE
EXTENSION COURSES

The following session, given by the Massachusetts Medical Society in co-operation with the Massachusetts Department of Public Health, the United States Public Health Service and the Federal Children's Bureau, has been arranged for the week beginning December 16.

FRISTOL NORTH

Thursday, December 19, at 4 p.m., at the Morton Hospital Taunton. Gonococcal Infections in the Armed Forces and the Civil Population. Instructor Oscar F. Cox. Lester E. Butler, *Chairman*.

DEATHS

GAFFNEY — MARY E. GAFFNEY, M.D., of Charlestown died December 5. She was in her sixty seventh year.

Dr. Gaffney received her degree from Tufts College Medical School in 1907, and was a former member of the staff of the Rhode Island State Sanatorium, Wallum Lake. She was a former member of the Massachusetts Medical Society and had retired from active practice.

MELLUS — EDWARD MELLUS, M.D. of Newton, died December 7. He was in his sixty ninth year.

Born in Zumbrota, Minnesota, he attended Worcester High School and Harvard College, and received his degree from the Harvard Medical School in 1903. He was a member of the Massachusetts Medical Society and the American Medical Association. He was also a member of the Newton Board of Health, a member of the staff of the Newton Hospital, a former member of the city planning board and a member of the New England Society of Psychiatry. At the time of his death he was treasurer of the Middlesex South District Medical Society.

Dr. Mellus maintained a sanatorium in Newton until 1929 when he retired from active practice.

Two sons and a daughter survive him.

MISCELLANY

CHAPTER OF ALPHA OMEGA ALPHA
AT TUFTS

On December 2, six members of the faculty and ten fourth year students at Tufts College Medical School were initiated as charter members of Beta Chapter of Alpha Omega Alpha, the national honorary medical society. Dr. Walter L. Biering, former president of the American Medical Association and national president of Alpha

Omega Alpha, conferred the charter. It was accepted on behalf of the school by Dean A. Warren Stearns. Certificates and keys were presented to the initiates by Dr. Josiah J. Moore, national society secretary.

Guests were Dr. Reginald Fitz, Dr. Walter B. Cannon, Dr. Henry A. Christian and Robert S. Grier, of Harvard Medical School, Dr. Hardy A. Kemp, dean of the University of Vermont Medical School, and President Leonard Carmichael, of Tufts College. Dr. Hyman Morrison, professor of clinical medicine, served as chairman of the faculty committee on installation.

The faculty initiates were as follows: Dr. David D. Berlin, professor of clinical surgery; Dr. Abraham Myerson, professor of neurology, emeritus; Dr. Dwight O'Hara, professor of preventive medicine; Dr. Alonzo K. Paine, professor of obstetrics; Dr. Louis E. Phaneuf, professor of gynecology; and Dr. Stearns, dean and professor of neurology.

The student initiates were as follows: Carl J. Antonellis, of Medford; Carroll J. Bryant, Jr., of Indian Orchard; George A. Dodge, 2d, of Brookline; Clement S. Dwyer, of Boston; Jesse G. Garber, of Brookline; Herbert F. Hager, of Providence, Rhode Island; Alfred Kant, of Cranston, Rhode Island; Arthur N. Kelly, of East Boston; John L. O'Hara, of Newton; and Raymond Yesner, of Boston.

INCIDENCE OF TUBERCULOSIS AMONG UNIVERSITY STUDENTS

A study of tuberculosis among students at Lund University in Sweden by Hedvall (The incidence of tuberculosis among students at Lund University. *Am. Rev. Tuberc.* 41:770-780, 1940) calls attention to the great risk of tuberculosis confronting young people and describes an excellent procedure for mass surveys of students. Of special interest is the discovery that the high incidence of tuberculosis among medical students was traced to the post-mortem examinations during their course in pathology. Abstracts of the study follow:

Pulmonary tuberculosis is characterized by an insidious protracted course and a prolonged absence of clinical symptoms. When such symptoms finally appear, the changes have frequently spread extensively in one or both lungs. It is essential, therefore, that pulmonary tuberculosis should, if possible, be diagnosed before the appearance of morbid symptoms.

On registration all students are required to go to the Student's Tuberculosis Bureau for an examination. On the first visit a careful history is taken, a tuberculin test by the Pirquet method and a sedimentation test are made, together with a fluoroscopic and radiographic examination. If the tuberculin test is negative, the students are retested by the Mantoux method with from 0.1 up to 1.0 mg. tuberculin. Only those who do not react to the 1.0 mg. dosage are considered negative.

A re-examination of all students is made at least once a year and follows the procedure of the original examination, with the exception of the x-ray examination, which is done every third year. However, an x-ray film is taken when the previous history, rate of sedimentation or fluoroscopic examination indicates something suspicious or when greater caution is necessary for some other reason. When the tuberculin reaction changes from negative to positive an x-ray examination is made every third month during the first year after the primary infection and every six months during the second year, even if no changes have been demonstrated. On the other hand, if any changes are observed they are followed by means of x-rays at intervals of a few weeks or months, irrespective of expense.

Altogether 3336 persons were examined; 638 were medical students, 1367 philosophy students, 409 theology students, 488 law students. To these were added 434 probationary nurses at the South Sweden School for Nurses. They were included to obtain a comparison with the medical students, since both these groups are undoubtedly exposed to a certain risk of tuberculous infection.

Among those examined, 133, or approximately 4 per cent, were found to have active tuberculosis. Of the 133 cases, 47 were tuberculin negative and had normal lung x-ray films when entering the university or school for nurses; 43 had been infected at some period of their lives, since they were tuberculin positive on first examination but were radiologically sound; and the remaining 43 were tuberculin positive and did not show a normal x-ray picture of the lungs on first examination. Some of these already had tuberculosis, but others did not develop it until later.

In general, the tuberculous changes were progressive and significant. Of the 47 patients who showed no evidence of tuberculosis on entrance, there developed 14 cases of pulmonary tuberculosis, as well as cases of erythema nodosum, exudative pleurisy, tuberculous peritonitis and milary tuberculosis, with 2 deaths.

Of the 43 patients in the second group who were tuberculin positive but radiologically sound on first examination, 37 developed pulmonary tuberculosis, 2 tuberculosis of the hilar lymph nodes, and 4 pleurisy. One of the cases of pleurisy developed pulmonary tuberculosis as a complication, and the patient died.

Of the 133 cases of tuberculosis found in the period from 1930 to the end of the 1937 spring term, 110 were among the university students and 23 among the nurses. Ninety-five students and 15 nurses are at present fit for work. Of the other patients, 9 have died, 5 are unfit for work and 9 are still at the sanatorium.

It is of interest, however, to know not only the number of cases found and how they developed, but also the frequency of the disease in the different groups, as shown in the table:

	No. OF PERSONS EXAMINED	No. OF CASES OF TUBERCU- LOSIS FOUND	PERCENTAGE
Medical students	638	72	11.3
Philosophy students	1367	17	1.2
Theology students	409	12	2.9
Law students	488	9	1.8
Nurses	434	23	5.3

These figures indicate that both medical students and probationary nurses are exposed to a considerable risk of tuberculous infection.

During the first year, no case of tuberculosis was found among the medical students. In the second year 4 cases were detected and during the third to the fifth year 10 cases each year. From the sixth to the ninth year only 6, 4, 2 and 1 cases respectively were diagnosed. Thus, most of the tuberculous cases were discovered during the third to the fifth year of study, a period which coincides with the last course before and the first course after the beginning of the practical training at the hospital. Since the medical students live under practically the same conditions as other students at the university, the high tuberculosis morbidity among them must be due to a risk of infection to which they alone are exposed.

Quite a number of the medical students are primarily infected before they begin their hospital training course and, therefore, some course taken before this training must be significant. The medical students themselves

have for a long time suspected that the course in general pathology taken before the hospital duty, and lasting one year constitutes a danger of tuberculous infection. In at least 16 cases, there is a significant connection between the course of general pathology and the appearance of the primary infection. In the other cases the primary infection occurred either before or after the pathological course during the training at the hospital.

The infection acquired during the course in pathology may have originated from fellow students or physicians. The probability of this happening was, however, carefully excluded. For this reason, thorough and repeated examinations of the autopsy rooms were made for the presence of tubercle bacilli. Samples were taken from towels, trays, dust on the autopsy tables and in the rooms, and it was found that in spite of all precautions during the post mortem examinations, tubercle bacilli were discovered when an examination was made twenty-four hours after a necropsy examination of a person with pulmonary tuberculosis. In addition to guinea pig inoculations, suitable cultural experiments were made to obtain a quantitative idea of the presence of tubercle bacilli on the objects and in the rooms examined.

As a result of these examinations, more stringent precautions in disinfecting the autopsy rooms were taken and finally it was agreed, at least for the present to limit the necropsy examinations of tuberculous patients as much as possible. The results of the latter step are as yet available only for two terms. Nevertheless, examinations showed that for the first time all tuberculin negative reactors at the beginning of the course were also negative at the conclusion of the course. The investigation is being continued and the definite result awaited but the author believes that he is justified in expressing the view that excessive tuberculous morbidity among medical students can be reduced by taking special precautionary measures against tuberculous infection in hospitals and in rooms in which necropsy examinations of tuberculous subjects are performed.

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR OCTOBER, 1940

DISEASES	OCTOBER 1940	OCTOBER 1939	FIVE YEAR AVERAGE*
Anterior poliomyelitis	7	21	58
Chicken pox	491	333	339
Diphtheria	22	24	19
Dysentery bacillary	842	823	770
German measles	21	165	39
Scarlet fever	27	40	30
Cornitis	374	474	499
Lobar pneumonia	218	157	237
Measles	619	291	210
Neisseria meningitidis	5	5	7
Mumps	199	91	206
Paratyphoid B fever	3	3	2
Scarlet fever	265	19	348
Syphilis	394	464	453
Tuberculosis pulmonary	256	238	259
Tuberculosis other forms	35	32	32
Typhoid fever	3	4	8
Undulant fever	3	4	6
Whooping cough	645	346	419

*Based on figures for preceding five years

RARE DISEASES

Actinomycosis was reported from Swampscott, 1, to
tal, 1
Anterior poliomyelitis was reported from Monterey, 1,
Northampton, 1, Russell, 1, Springfield, 1, Wareham, 1,
Worcester, 2, total, 7
Anthrax was reported from Lynn, 1, total, 1
Diphtheria was reported from Boston 3, Cambridge, 2,
Chicopee, 2, Cohasset, 1, Fall River, 3, Lawrence, 1, Mel-

rose, 1, New Bedford, 1, Somerville, 4, Westboro, 2,
Worcester, 2, total, 22

Dysentery, bacillary, was reported from Boston, 6, Cambridge, 5, Danvers, 5, Lowell, 4, Taunton, 1, total, 21

Meningococcus meningitis was reported from Gloucester, 1, Natick, 1, Pittsfield, 1, Reiding, 1, Uxbridge, 1, total, 5

Paratyphoid B fever was reported from Boston, 1, Danvers, 1, Worcester, 1, total, 3

Pellagra was reported from Boston, 2, Greenfield, 1, total, 3

Septic sore throat was reported from Beverly, 1, Boston, 5, Cambridge, 2, Greenfield, 1, Lynn, 1, Somerville, 1, Sturbridge, 3, Weston, 1, total, 15

Tetanus was reported from Framingham, 1, total, 1

Trachoma was reported from Plymouth, 1, total, 1

Trichinosis was reported from Cambridge, 1, Framingham, 1, Lynn, 1, Webster, 1, Worcester, 1, total, 5

Typhoid fever was reported from Athol, 1, Boston, 2, Chelsea, 1, Malden, 1, Waltham, 2, Worcester, 1, total, 8

Undulant fever was reported from Shrewsbury, 1, Webster, 1, Whitman, 1, total, 3

Anterior poliomyelitis continued to show low incidence. Diphtheria, measles, whooping cough, chicken pox and tuberculosis (other forms) were reported above the five year averages.

The incidences of meningococcus meningitis and undulant fever were not remarkable.

Typhoid fever was reported at a figure equal to that of the five year average.

Lobar pneumonia, pulmonary tuberculosis, mumps scarlet fever and German measles were reported below the five year averages.

Dog bite was reported at a record high figure for the third consecutive month. Animal rabies showed an increased incidence with active foci in Cohasset, Attleboro, Boston and Hingham.

REPORT OF MEETING

BOSTON ORTHOPEDIC CLUB

A regular meeting of the Boston Orthopedic Club was held at the Boston Medical Library on October 21, with Dr. Augustus Thorndike, Jr., presiding. The speaker of the evening, Dr. Fuller Albright, discussed the subject, 'Metabolic Bone Disease'. It was initially emphasized that any metabolic disease is generalized and not, like infection or tumor, merely disseminated. At times this generalized character may be masked, particularly if the disease is more marked in localized areas. It has been found that the absence of the lamina dura of the teeth is a good index of generalized bone disease.

Dr. Albright briefly discussed the normal metabolism of bone, in which both addition and subtraction are taking place at the same time. Probably only 1 per cent of all bone is being thus actively metabolized at any time, however. The loss of calcium phosphate from bone to the surrounding fluid is governed by physicochemical laws, and the simultaneous deposition of this compound is probably due to an elevation of the phosphate ion brought about by the enzyme phosphatase.

The discussion was limited to those conditions in which too little bone is formed. In the first type of disease there is too little bone formation as a result of osteoblastic hypoplasia—namely osteoporosis. This condition may be found in prolonged immobilization in a cast, which

6 45 p.m. Massachusetts Society of Examining Physicians. Copley-Plaza Hotel, Boston.

*8 p.m. New England Society of Physical Medicine Hotel Kenmore, Boston.

THURSDAY, DECEMBER 19

*8 30 a.m. Combined clinic of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital, at the Peter Bent Brigham Hospital.

*9-10 a.m. Medical conference. Joseph H. Pratt Diagnostic Hospital.

FRIDAY, DECEMBER 20

*9-10 a.m. The Banti Syndrome Dr. L. K. Diamond Joseph H. Pratt Diagnostic Hospital

SATURDAY, DECEMBER 21

*9-10 a.m. Hospital case presentation Dr. S. J. Thannhauser Joseph H. Pratt Diagnostic Hospital

*Open to the medical profession.

DECEMBER 27 — Danvers State Hospital, clinicopathological conference Page 999.

DECEMBER 27-29 — National Convention of the Association of Medical Students, Boston

JANUARY 3, 1941 — Massachusetts Memorial Hospitals, staff meeting Page 999.

JANUARY 4 — American Board of Obstetrics and Gynecology. Page 787, issue of November 7

JANUARY 9 — Pentucket Association of Physicians Page 263, issue of August 15.

JANUARY 13, 14 — Third Annual Congress on Industrial Health. Page 999

FEBRUARY 20-22 — American Orthopsychiatric Association, Inc. Page 999

MARCH 8 — American Board of Ophthalmology Page 201, issue of August 1.

APRIL 21-25 — American College of Physicians Page 1065, issue of June 20.

MAY 21, 22 — Massachusetts Medical Society, Boston

JUNE 2-6 — American Medical Association Cleveland, Ohio.

DISTRICT MEDICAL SOCIETIES

ESSEX SOUTH

JANUARY 8 — Visceral Pain and Its Relief Dr. James C. White. Danvers State Hospital, Hathorne.

FEBRUARY 5 — Gastric and Duodenal Ulcer Diagnosis and treatment Dr. Arthur Allen. Lynn Hospital

MARCH 5 — X-ray in Heart Disease Dr. Merrill C. Sosman. Essex Sanatorium, Middleton.

APRIL 2 — Pediatric Problems in General Practice. Dr. Joseph Garland. Addison Gilbert Hospital, Gloucester

MAY 14 — Relation of the Doctor to the Law. Mr. Leland Powers New Ocean House, Swampscott.

FRANKLIN

JANUARY 14.

MARCH 11.

MAY 13.

Meetings will be held at 11 a.m. at the Franklin County Hospital, Greenfield.

NORFOLK

JANUARY 28 — Carney Hospital

FEBRUARY 25 — Medicolegal meeting 8 30 p.m. Hotel Puritan, Boston.

MARCH 25 — To be announced.

MAY 8 — Censors' meeting. Hotel Puritan.

SUFFOLK

JANUARY 29 — Page 604, issue of October 10.

APRIL 30 — Page 604, issue of October 10.

WORCESTER

JANUARY 8, 1941 — Worcester City Hospital, Worcester.

FEBRUARY 12 — Worcester State Hospital, Worcester.

MARCH 12 — Memorial Hospital, Worcester.

APRIL 9 — Hahnemann Hospital, Worcester.

Supper at 6 30 p.m. followed by a business meeting and scientific program.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books

that appear to be of particular interest will be reviewed as space permits. Additional information regard to all listed books will be gladly furnished on request.

Haemorrhoids and Their Treatment: The varicose drome of the rectum. By Kasper Blond, M.D. (Vien formerly first assistant, Rothschild Hospital, Vienna), honorary consulting surgeon, Municipal Hospital, Vienna. Translated by E. Stanley Lee, M.S., F.R.C.S., honorary assistant surgeon, Westminster Hospital. 8°, cloth, 140 pp., with 49 illustrations. Baltimore: Williams and Wilkins Company, 1940. \$4.50.

A Review of the Psychoneuroses at Stockbridge. Gaylord P. Coon, M.D., chief medical officer, Boston Psychopathic Hospital; and Alice F. Raymond, A.B., statistician, Department of Child Hygiene, Harvard School of Public Health. 8°, cloth, 299 pp., with 66 tables and 2 figures. Brattleboro, Vermont: E. L. Hildreth & Company, Incorporated, for Austen Riggs Foundation, Incorporated, Stockbridge, Mass., 1940. \$2.00 (obtainable from the Foundation).

Synopsis of Materia Medica, Toxicology and Pharmacology. By Forrest Ramon Davison, B.A., M.Sc., Ph.D., M.B., assistant professor of pharmacology, School of Medicine, University of Arkansas. 12°, cloth, 633 pp., with 45 illustrations. St. Louis: C. V. Mosby Company, 1940. \$5.00.

In Search of Complications: An autobiography. By Eugene de Savitsch, M.D. Foreword by Arthur Krock. 8°, cloth, 396 pp. New York: Simon and Schuster, 1940. \$3.00.

Bacillary and Rickettsial Infections, Acute and Chronic: A textbook. Black Death to White Plague. By William H. Holmes, M.D., professor of medicine, Northwestern University Medical School, and chairman, Department of Medicine, Passavant Memorial Hospital, Chicago. 8°, cloth, 675 pp. New York: Macmillan Company, 1940. \$6.00.

The Treatment of Diabetes Mellitus. By Elliott P. Joslin, M.D., Sc.D., medical director, George F. Baker Clinic, New England Deaconess Hospital, clinical professor of medicine emeritus, Harvard Medical School, and consulting physician, Boston City Hospital; Howard F. Root, M.D., physician, New England Deaconess Hospital, consultant in medicine, Eastern Maine General Hospital, Massachusetts State Infirmary, Tewksbury, and Middlesex County Sanatorium, and instructor in medicine, Harvard Medical School; Priscilla White, M.D., physician, New England Deaconess Hospital, and instructor in pediatrics, Tufts College Medical School; and Alexander Marble, M.D., physician, New England Deaconess Hospital, and instructor in medicine, Harvard Medical School. Seventh edition, thoroughly revised. 8°, cloth, 783 pp., with 117 tables. Philadelphia: Lea & Febiger, 1940. \$7.50.

Diseases of the Urethra and Penis. By E. D'Arcy McCrea, M.D., M.Ch. (Dub.), F.R.C.S. (Eng.), honorary surgeon, Salford Royal Hospital, Manchester (England). 8°, cloth, 306 pp., with 181 illustrations. Baltimore: Williams & Wilkins Company, 1940. \$6.50.

Psychiatry for the Curious. By George H. Preston, M.D., commissioner of mental hygiene for the State of Maryland. 8°, cloth, 148 pp., with 17 sketches. New York: Farrar & Rinehart, Incorporated, 1940. \$1.50.

The New England Journal of Medicine

Copyright 1940 by the Massachusetts Medical Society

VOLUME 223

DECEMBER 19, 1940

NUMBER 25

A REVIEW OF THE CAMPAIGN TO ERADICATE TUBERCULOSIS*

HENRY D CHADWICK, MD

WALTHAM, MASSACHUSETTS

ONE of the greatest achievements of the twentieth century will be the subjugation of tuberculosis. We are far enough along in the campaign that started when this association was organized thirty six years ago to be quite certain that victory eventually will be won, but we must not be too complacent, for we are dealing with a very resourceful opponent who will take advantage of any weakening of our defenses to make a counter-attack. The small group that met in Baltimore and founded the Association for the Study and Prevention of Tuberculosis were brave and determined men. They were living at a time when tuberculosis was causing the death of more than 150,000 persons annually in the United States. This was at the rate of 200 per 100,000 population. The tubercle bacillus had been known to be the causative agent for twenty two years. Tuberculin, heralded as a cure, had been discredited. About 9000 beds were being used for tuberculous patients, but most of them were for terminal cases. The notable exceptions were the comparatively few beds at the Adirondack Cottage Sanitarium, carefully nurtured by Dr. Edward L. Trudeau, and the small Sharon Sanatorium in Massachusetts, brought into being by his disciple, Dr. Vincent Y. Bowditch. Out of their experience the Rutland State Sanatorium was founded in Massachusetts in 1898. The importance of this event was that it was the first time the civic responsibility for the treatment of tuberculosis had been recognized and accepted by any legislative body.

The name selected for the organization, Association for the Study and Prevention of Tuberculosis, was descriptive of its purpose. The founders recognized that, because little was known about the incidence of infection, methods of transmission, measures of prevention or principles of treatment, the systematic study of the disease was of first importance.

In the early years of the association the stress was put on treatment, later on prevention, then

on health education and on case finding, these four, together with research, make up the forces that under one co-ordinated command are now in the field doing valiant work against the disease. Much has been accomplished. The death rate has dropped 76 per cent in forty years. Critics take pleasure in reminding us that tuberculosis mortality declined steadily before Koch discovered the bacillus or any concerted public health measures were taken to control it. It is true indeed that we cannot take all the credit for this improvement, as is evident from a study of the vital statistics in Massachusetts which go back to 1842. In the first annual report published that year the registrar lists consumption as causing 22 per cent of all deaths. Let us compare two forty year periods, one prior to 1900, the other subsequent to that date. From 1860 to 1899 the rate declined from 444 to 254, a drop of 43 per cent. From 1900 to 1939 the rate declined twice as much, from 253 to 36, a drop of 86 per cent. We may assume that the same favorable factors that existed in the period prior to 1900 have continued to operate, and that to them have been added the resources of the health and welfare agencies brought to bear directly and indirectly on the control of the disease. The effect has been to accelerate greatly the rapidity of the fall of tuberculosis from the commanding position it formerly occupied.

We must not be content with what has been accomplished, we have far to go before our objective is gained. Sixty thousand lives a year even now are taken by the tubercle bacillus. The goal of eradication can be visualized in the distance, but it is two generations away if we proceed at our present rate. Our campaign is one of attrition, slow but certain of attaining the objective. In the four decades since 1900 the reduction in mortality from tuberculosis in the United States was 20 per cent in the first, 22 per cent in the second, 33 per cent in the third and 34 per cent in the fourth. We have been quite pleased with this progress and may even have boasted about it. Yes, there are some who go so far as to say that there is no need of building more sanatoriums, that

*The presidential address delivered at the thirty-sixth annual meeting of the National Tuberculosis Association, Cleveland, Ohio, August 1939.

there are enough beds now, and that before long some other use will have to be found for those that we now have. With so many other major health problems to face and solve, we need not be seriously concerned with this contingency. Even now there is a growing demand for institutions to care for patients with cancer, rheumatic heart disease, diabetes and arthritis. For the present, however, a surplus of beds for conversion to other purposes does not exist, nor will it for some years to come.

The tuberculosis mortality, as we have just reviewed it, dropped 33 per cent and 34 per cent respectively in the last two decades. Let us assume, therefore, that this average decline of approximately one third every ten years can be maintained. In that event, the tuberculosis death rate would be 32 in 1950, 21 in 1960, 14 in 1970; forty years from now, in 1980, a rate of 9 or 10 may be anticipated. The bells that ring in the year 2000 may sound the death knell of the tubercle bacillus.

Do you not agree with me that this seems a leisurely way to dispose of tuberculosis? A study of ancient records, however, shows that the disease has been decimating the ranks of mankind for at least four or five thousand years. Its extermination, therefore, in one century of effort would be indeed quite a creditable achievement. Saint Paul, writing to the Hebrews, said: "Now, faith is the substance of things hoped for, the evidence of things not seen." Our faith, then, warrants our believing that the twentieth century will mark the end of tuberculosis. Furthermore, we are warned by Saint James that "faith without works is dead." It is evident, therefore, that work as well as faith will be needed, and if both are used judiciously in the fullness of our knowledge, we can shorten materially the time that we must serve as host to this unwelcome parasite.

The United States Department of Agriculture has led the way in a successful campaign to eradicate bovine tuberculosis. In about twenty years it has overcome a growing menace that seriously threatened the dairy industry. By legislation supported by public opinion a systematic plan was put into effect that involved the repeated testing of all cattle and the slaughter of the positive reactors, with the result that bovine tuberculosis has been practically wiped out. In the early years of this work sporadic testing was done at the request of the individual owners. Segregation of infected animals on farms with clean cattle was tried without success. Infection would spread in spite of elaborate measures taken to prevent it; the herds of unco-operative farmers would trans-

mit the disease to the clean herds of their progressive neighbors. Mandatory legislation requiring all cattle in a given area to be tested was finally necessary to overcome this fault, and also to prevent the shipment of animals from infected sections into accredited areas. In other words, absolute compliance was required before eradication could be accomplished. Lessons can be learned from the veterinarians that are applicable to an eradication program directed against the human type of the bacillus.

The human and bovine bacilli are blood brothers: their method of attack is the same, they wear the same armor, they yield only at death. The success of the agriculturists is due to their persistence along one line: a direct attack on the bacillus with no quarter given, even when this involves the destruction of the host.

Our problem is more complex. We can search out the bacillus, but when we find it we cannot destroy the carrier. We must temporize, we must educate, and by slower methods of prevention we must try to protect others. In our attempt to cure, we often succeed and thus do much to limit the spread of infection. To slaughter human beings on the pretext of affording others protection is deemed illegal and is barred, except in modern warfare. The substitute measure is segregation in institutions. My plea, therefore, is for more beds—one for every tuberculous patient who should have one. The needs of two groups, the patients and the public, should be recognized. Patients are entitled to the best treatment; the public, represented by patients' families and their business and other associates, have a right to protection. Both are served when patients are sent to sanatoriums.

These institutions must be so situated that they are accessible to both patients and their friends and families. They must be made so attractive that patients will remain long enough to receive permanent benefit. Voluntary segregation for treatment is our aim—not in a concentration camp with its attendant discomfort and discontent, but among pleasant surroundings that will compensate in part for the sacrifice made by the patient in leaving home. We have successfully emphasized the advantages of case-finding in recent years. It has kept the institutions filled and has demonstrated the need for enlarging present sanatoriums and building others. But case-finding activities carried beyond this point serve no useful purpose. They are quite futile unless beds are available for the treatment and segregation of patients.

How many beds should we provide to meet this need? There are 732 institutions with a capacity

of 90,000 beds listed in 1938, or approximately 1.5 beds per annual death. They are distributed very unevenly over the country; a few states have enough, but many have too few. It has been shown that a minimum of 2 beds for each annual death is needed where a good case-finding program is carried on and well-equipped institutions are available. Thirteen states have exceeded this quota, and four have as many as 3 beds per death. Far down the list are fourteen states that have not provided even 1 bed per death. If beds in federal hospitals are excluded, five more should be added to this group, making nineteen of the forty-eight states with only meager or almost negligible accommodations. The tuberculosis death rates in thirteen of those states exceeds the average for the country as a whole. The National Tuberculosis Association through its affiliated state organizations should wage a persistent campaign for more sanatoriums in these states to bring them up to the minimum standard.

Here is where the hardest blows can be struck against tuberculosis. The early-diagnosis campaign in these states may well take a holiday while bed-finding takes the place of case-finding as a major activity. Efforts should be centered on arousing public opinion to a point where the people will insist that suitable hospitals are provided for tuberculous patients. Within the limit of their resources people should tax themselves to finance these institutions, both for construction and for maintenance. In states where the property valuation is low, grants-in-aid should be made available from federal funds. Tuberculosis is a pandemic disease and therefore a national problem. If ever a good-neighbor policy is warranted, this is the place to put it into action. Such aid should not be budgeted as charity but as insurance to be expended for self-protection and the common good. When beds for patients are insufficient in number and when waiting lists build up, the delay inevitably costs some patients their chance of cure.

The community is not protected from open cases if these patients remain at home or return there before they cease to be infectious. When a state fails to provide sufficient beds, it is committed to a plan that is wasteful, ineffective and costly. Tuberculosis is controlled little, if at all, by treating only a small percentage of patients and leaving many open cases in the community to sow the seed for another crop of victims, who in their turn will be needing care. If we admit to the sanatoriums only the hopeful cases, we leave in the homes the most active spreaders of disease; and if we admit only the advanced cases to give them terminal care, we leave in the homes the

hopeful cases until they in turn need terminal care. The grist is always waiting at the mill. The expense goes on, the march of death is unimpeded. Halfway measures will not suffice to eradicate tuberculosis.

The number of beds needed in a state or community can be computed with fair accuracy by multiplying the number of annual deaths by ten and dividing the result by four. There are 10 active cases of tuberculosis for each death, and 25 per cent of them need and will accept institutional care.

This has been the experience where good case-finding programs are carried out and well-conducted institutions are available to the patients. The maintenance expense in large part must be borne by the public, for few patients are able to pay the cost of treatment. This is most important, because it is useless to build hospitals and then keep patients from obtaining the benefit by putting up a sign announcing that "All must pay who enter here." Tuberculosis is not always a poor man's disease, but savings of considerable amount which a few may possess at the beginning of their illness are expended in most cases long before the course of treatment comes to an end.

Applying our formula to the United States to find the number of patients with active tuberculosis, let us multiply the 60,000 deaths by ten; the result is 600,000, which is approximately correct. The 25 per cent who need and will accept hospitalization will require 150,000 beds. There are now but 90,000, which means that 60,000 more beds are needed to provide a full complement. These are required in order to wage our war against tuberculosis more effectively. It is an attainable objective. The ratio is 2.5 beds per death, and eight states now have that number. If we include the beds in federal hospitals,—which is the logical thing to do because we are planning on a national basis,—there are nine states with this quota. They are Colorado, Connecticut, Massachusetts, Michigan, Minnesota, New Mexico, North Dakota, Rhode Island and Wisconsin. Some others, quite close to this ratio, will soon reach it. Many other states are financially able to comply and should do so. Some states need assistance. The President's plan as represented in a bill to construct hospitals in areas that are unable to provide them is broad enough to include institutions for the tuberculous. A subsidy to help maintain them should be provided so that they may be kept filled to capacity. Tuberculosis is a migratory disease and pays no heed to state lines; therefore, its control should not be the sole responsibility of a state but should be shared by the

national government. Many millions of federal funds have been used during the past few years to pay farmers for not raising pigs, grain and potatoes. Why not use such funds to pay for not raising tubercle bacilli? If a sum equal to a small percentage of such appropriations could be expended for much needed sanatoriums and their maintenance, the crop of tuberculosis would be curtailed, with benefit to the entire population of the United States.

Many additional beds for tuberculous patients placed where most needed should be item Number 1 on our agenda. Health education as it applies to tuberculosis is item Number 2. This has a broad connotation with boundaries that cannot be clearly defined. Everything that tends to improve living conditions of that part of the population who are forced by circumstances to reside in crowded quarters on a diet inadequate in quality or quantity contributes toward the eradication of tuberculosis. In this class of subsidiary factors are better housing, adequate wages and regulation of hours of labor, all of which are highly valuable allies, since they operate beneficently on the fraction of the population that is most vulnerable to tuberculosis. It is unnecessary to speak in much detail of what may be called direct health education within our field; for example, the cause of the disease, how it is transmitted from one to another, the incidence of infection and disease, the susceptibility of certain age and economic groups and the importance of x-ray examination in early diagnosis, all of which are the stock in trade of our craft. So familiar to us are these matters of what ought to be common knowledge that we deceive ourselves, and take for granted that our teaching has accomplished its purpose and that the people as a whole are well informed. We must not jeopardize our favorable position through overconfidence. With the weapons now at our command wielded by the agencies now in the field and working in close harmony, we may expect continued progress toward our goal.

The ultimate surrender of the tubercle bacillus, however, is two generations away, unless new developments in treatment come to our aid. This surrender may be brought about more quickly by discoveries made in the fields of chemotherapy and nutrition. Research in both fields is yielding rich returns. No one could have foretold the brilliant results now being attained by the use of recently discovered drugs that seem to be specific for infections with the pneumococcus, the streptococcus, the gonococcus and the meningococcus. These are diseases that have up to this time resisted the best efforts of physicians to cure or to control. In Massachusetts the mortality from

pneumonia for an eighty-year period prior to 1936 declined but 10 per cent; during the same period tuberculosis declined 90 per cent. It appears from this that pneumonia is a harder problem to control than is tuberculosis. Yet suddenly from the research laboratories comes a specific that cures pneumonia. May we not have faith that one will be found for tuberculosis? The other field of research that has yielded rich returns has been nutrition. A group of pathological enigmas, such as pellagra, beriberi, scurvy and rickets, have been found to be caused by the lack of some vital element in the food. These deficiency diseases now have their vitamins that restore to health people who were chronic invalids or were considered hopelessly ill. Possibly the chemists will find a substance that can be used to enhance the resistance of tissues to the tubercle bacillus so that when that invader appears its position will become untenable.

We know that people vary widely in their susceptibility to tuberculosis. The majority have enough resistance to withstand infection without succumbing to disease. This is obvious from the fact that although contact with the tubercle bacillus is a common experience, only about 5 per cent (4.6 per cent in 1938) of all deaths are due to tuberculosis. Another but unknown percentage of patients develop disease of a chronic type from which they recover. In some the bacillus dies out without causing a demonstrable lesion. At the other extreme are cases that run so acute a course that the lung tissue seems literally to melt away as if exposed to the action of some very active enzyme. This mysterious substance, which renders certain persons immune or less susceptible, is inherent in individuals and in some families. The physicians of another day ascribed this trait to a good constitution. We have no better name. Is the resistant individual endowed with a vitamin X which is wanting in susceptible persons? If so, tuberculosis may be classed as a deficiency disease, and the remedy may be found by the biochemists when they isolate this elusive substance and make it available for use. This would be an addition of inestimable value to our defensive measures.

While the chemists of various types and interests are delving in their laboratories, we plodders in the broad fields of physic and education must continue to use the methods that have been proved sound and true. Yet we must be alert and responsive as new procedures are developed, changing our tactics if necessary and varying our course to keep in line with the changing times.

With all the research work being carried on, it seems not unlikely that sooner or later a dis-

covery will be made that will revolutionize the treatment of tuberculosis. I have faith that this will come to pass. Some years ago I was superintendent of a sanatorium for children. The ward for the patients under ten years of age was located near the woods. One day at lunch time it was discovered that two seven-year-old boys named Micky and Jaky were missing. Search was made for them all the afternoon without success. The sun went down and it was getting dark before the two wanderers appeared. Their tear-stained faces with an overlay of grime showed that they had had a difficult day. They were tired but overjoyed to be back and were eager to tell of their adventures. In their play they had wandered into the woods until they had suddenly realized that the buildings were out of sight and nothing familiar could be seen. After walking about for a long time trying to find their way, they sat down and fell asleep so soundly that the shouts of the searchers did not arouse them. When they awoke it was getting dark and they were frightened at the prospect of spending the night

in the woods. "What did you do then?" they were asked. Micky replied, "I knelt down by the trunk of a big tree and prayed." "What did *you* do?" Jaky was asked. "I climbed the tree," he answered, "and when I got near the top I could look over the other trees and see the lights of the sanatorium. It was not very far away and we beat it in." This is an example of the effectiveness of faith and work going hand in hand—not one without the other.

The National Tuberculosis Association has been wandering about in an unexplored wilderness for thirty-six years. Although making some false starts, as could be expected with no blazed trails to follow, it has made great progress but still finds much work to be done. When we clear away the underbrush that obscures our vision, or when we reach a high point that will serve as a tall tree from the top of which we may look over the intervening country, we too may find that we are not far from the promised land, and that we can reach it in one generation instead of two.

Middlesex County Sanatorium

THE CONTRACEPTIVE SAFE PERIOD

A CLINICAL STUDY

STEPHEN FLECK, MD,* ELIZABETH F. SNEDEKER, B.A.,† AND JOHN ROCK, MD‡

BROOKLINE, MASSACHUSETTS

PERIODIC sterility and fertility during the female sex cycle is an old Biblical concept, the physiology of which has but recently been explained. Ogino¹ and Knaus,² having studied independently the ovarian cycle, recommended the use of this periodicity for the control of fertility. The so-called "rhythm method of contraception," based on their theories and on the research of many others, is deliberate continence during the fertile period of the female cycle.

This method has been applied in the Rhythm Clinic of the Free Hospital for Women in Brookline, which at the present writing is the only free clinic in Massachusetts available to patients desiring contraceptive advice. The clinic was opened in June, 1936, and this report covers the work from then until March 31, 1940. Clinic sessions are held once a week.

METHODS AND MATERIAL

The calculation of safe and fertile periods for each patient is made as follows. The sixteenth

to twelfth days inclusive before the next expected menstruation constitute for us the period during which ovulation may occur.^{2,3} An admittedly generous allowance of three days before and after this period is added for the viability of spermatozoa^{4,5} and susceptibility of ova,^{4,6} respectively. The theory may be expressed thus. The fertile period extends from and including the nineteenth day before the *earliest* likely menstruation up to and including the ninth day before the *latest* likely menstruation. In each case the apprehended dates of menstruation are derived from the patient's written record of previous catamenial dates.

At the first visit a complete medical, social, marital and obstetric history is taken. Physical examination is made at this time and repeated as often as indicated. The method is explained carefully, and each patient is given a calendar on which are crossed out the days of the theoretical fertile period. The patient is asked to mark the day of her subsequent menstruation as well as the dates of coitus. Every month, immediately following menstruation, these calendars are checked at the clinic, and safe and fertile periods are determined for the en-

*Formerly assistant Fertility Clinic, Free Hospital for Women.

†Social worker, Fertility Clinic, Free Hospital for Women.

‡Research associate in obstetrics and instructor in gynecology, Harvard Medical School, visiting surgeon, Free Hospital for Women.

suing cycle. Before the rhythm for any patient can be calculated, a minimum of three previous catamenial dates is required.

Any patient whose menstrual cycles vary so widely in length as to suggest intermittent failure of ovulation⁷ is advised not to rely on the clinic. Women recently delivered, as well as those still lactating, are urged to delay attendance until they have had at least three cycles of average and similar length.

It has proved advantageous to both patients and the clinic secretary to have the calendars mailed to the hospital on the day of menstruation, rather than to depend on the patient's return to the clinic on the first available clinic day following menstruation.

Patients who have been using rhythm long enough to be able to apply the method themselves are advised to have their calendars checked every six months. If they neglect to communicate with the clinic for more than six months, a follow-up letter is sent, asking for information. After management by mail had been resorted to in preference to monthly visits by the patient herself, a much more consistent contact was maintained, the possibility of error diminished, and a closer follow-up became possible. Formerly, many patients were lost because of inability to keep in touch with the clinic, and errors due to misapplication of the method were more frequent. A few patients were discharged when it was thought that they were competent to make their own calculations.

Since the opening of the clinic, 225 patients have applied for treatment. The average age at the time of the first visit was 30.4 years, the ages ranging from nineteen to forty-three. Seventy-seven patients were foreign born, and 148 were American by birth. One hundred and ninety-eight patients were Roman Catholic, 22 were Protestant, 1 was Greek Orthodox, 1 was Jewish, and the religion of 3 was unknown.

The families of 149 patients were self-supporting. The families of 6 were receiving partial relief; the husbands of 9 were employed by the WPA, and the families of 42 had no income of their own. No data were available for the remaining 19 patients. Roughly, 25 per cent of the whole group were thus dependent on outside support of some sort.

It is interesting to note that over one third of the women were referred by hospitals (70 patients) and local physicians (11 patients). Fifty-seven patients were referred by the nurses of the Boston Community Health Association. Of the remainder, 33 patients were referred by social agen-

cies and 39 came to the clinic of their own accord or through the recommendation of friends or other patients. Five were sent to the clinic by priests. The sources of the remaining 10 are not known.

PATHOLOGICAL AND OBSTETRIC DATA

As has already been mentioned, all patients were subjected to physical examinations, and varied pathologic conditions were discovered. Some of these were obvious from the patients' histories, or constituted the reason for referral. The infrequency of the latter suggests a considerable reluctance on the part of doctors and clinics to refer patients whose health would be endangered by a subsequent pregnancy. Only 24 of our patients belonged in this category. These were 2 cases of malnutrition, 8 of tuberculosis, 5 of rheumatic heart disease, 5 of chronic nephritis and 1 each of hyperthyroidism, breast tumor, hydronephrosis and asthma. In addition to these 24, 4 patients were classified as psychoneurotics and 2 had untreated syphilis.

Other pathologic conditions of less importance were found in 141 patients. The commonest defects were chronic cervicitis (54 cases) and perineal lacerations (35 cases). A large number of insignificant and incidental conditions such as are found in any clinic population were diagnosed.

The whole group reported a total of 1004 pregnancies, of which only 113 were abortions. The latter occurred in 73 patients. According to statements made there were only 10 induced abortions. These figures are too low, since the thorough investigations of Taussig⁸ and of Wichl^{9,10} have shown that abortions are about twice as frequent as here indicated, and that between one and two thirds of all abortions are not spontaneous. The fact that reliable data on this subject cannot be obtained in a single time-limited interview has been stressed by the same authors.⁹⁻¹²

Of the pregnancies, 891 were full term, but at the present writing there are only 823 living children. The average number is 4.4, ranging in various families from one to fourteen children respectively. Ten patients had had no children or pregnancies. Eight patients had undergone fifteen cesarean sections, the maximum being four in the same patient. Three patients had had toxemia with one or more of their pregnancies, and 1 each had had placenta previa, tubal pregnancy and subinvolution.

RESULTS

Of the 225 patients who applied for treatment, 12 were rejected immediately because of irregularity of periods, and 6 were not treated because

they were found to be pregnant at the time of their first visit. Twenty four patients became pregnant while under treatment. Ninety five cases were closed for the reasons given below. Eighty-eight cases were active as of March 31, 1940.

Of the 207 accepted patients, 57 were treated from 6 months to 1 year, and 63 were treated longer than 1 year, that is, 120 for at least six months (Table 1).

Among the 207 patients actually cared for, there were 24 pregnancies. Three of these were planned, leaving 21 pregnancies that might be considered

TABLE 1 Duration of Treatment in Accepted Cases

STATUS OF PATIENT	DURATION OF TREATMENT				TOTAL CASES
	ONE VISIT	LESS THAN 6 MONTHS	6 TO 12 MONTHS	OVER 1 YEAR	
Active	5	24	26	33	88
Pregnant	0	3	4	17	24
Closed	27	28	27	13	95
Totals	32	55	57	63	207

failure of treatment: a gross uncorrected failure rate of 10 per cent. Fourteen of the undesired pregnancies, however, were due to failure of the patients to follow instructions. 10 patients neglected to keep in contact with the clinic for readjustment of their rhythm, made necessary by changes in menstrual habit, 4 patients had intercourse one or more times during the fertile period.* One patient became pregnant after miscalculation of her rhythm in the clinic. These 15 pregnancies can hardly be considered failure of the method, although they are due to inaccuracy in application. Deducting these 15 from the total of 21 pregnancies, we find only 6 pregnancies among 207 patients, giving a corrected failure rate of 2.9 per cent. These 6 patients became pregnant despite the fact that they had followed instructions of the clinic. Assuming the reliability of the patients' statements, they must be regarded as true failure of the method as contrasted to failure due to misapplication or miscalculation, and they present a definite challenge to the theoretical foundations of the Ogino-Knaus method. Since 2 of these patients with true failure had been treated for three and four months respectively, the remaining 4 constituted only 3.3 per cent of the 120 patients who were observed and treated for six months or more.

The histories of the 6 patients with true failures showed that their fertility was no greater than that of the whole group, nor did the length of their cycles vary any more from the norm than

did the cycles of other women. Only 3 of these patients had a mean deviation of more than 25 days (the average of the total group) in the length of successive cycles. It is therefore hardly justifiable to conjecture that some, if any, of these patients had frequent anovulatory cycles, which might disturb the theoretical relation between menstrual flow and ovulation. That such anovulatory menstruation occurs is generally accepted,⁷ although the possibility of ovulation outside the theoretical range of sixteen to twelve days before the subsequent menstruation is real, if not proved.^{7, 18}

In our series no pregnancies could be ascribed to gross irregularities in menstrual cycles. For further details of the 21 undesired pregnancies the reader is referred to Table 2.

There were 95 patients who discontinued treatment for a variety of reasons. It is difficult to compile an accurate list of these, for often a single couple may have had more than one such motive. Also, many of these patients were lost despite repeated letters and visits. Somewhat arbitrarily we have analyzed the group as in Table 3. Many of these patients were under treatment for only short periods, and in both the dissatisfied and lost groups, totaling 76 patients (37 per cent), almost half the patients had only one contact with the clinic (13 out of 29 dissatisfied, and 20 out of 47 lost). Only those patients who made a definite statement to that effect were classified as dissatisfied. Although the clinic follow-up facilities are limited, the high percentage of the lost cases is due in great part to unknown addresses, and failure to respond to repeated letters. It is reasonable to assume that most of these cases fall into the dissatisfied group.

It was necessary to stop the treatment of 2 patients because their periods were so irregular that no reasonably long period of safety could be calculated. Together with the 12 patients rejected at the time of their first visit for the same reason, they constituted 6.2 per cent of those who applied. However, the cycles of all the patients who discontinued treatment were even less irregular than were those of the active group. The mean deviation from the average cycle among the closed cases was only 21 days, as contrasted with 29 days for the patients still active to date.

Six patients had used the method only while waiting for operative correction of various gynecologic disorders which entailed sterilization.

Finally, 7 patients were discharged: 4 because they were familiar enough with the method to continue it without supervision, and 3 because they desired pregnancy.

* Even other patients who did not become pregnant also had had intercourse during the fertile period.

THE DIAGNOSTIC SIGNIFICANCE OF SEROUS FLUIDS IN DISEASE*

FRANKLIN K. PADDOCK, M.D.†

BOSTON

A SURVEY of the literature reveals surprisingly little published evidence to support the statements commonly made in textbooks of clinical pathology on the characteristics of pathologic serous body fluids. These dicta have usually been borrowed from earlier authors, who in turn have presented no basis for them. In routine clinical work, exceptions to traditional interpretations are so numerous that one is inclined to disregard laboratory studies of fluids, thus losing a valuable diagnostic aid, or to put too much faith in a determination that is liable to various errors. The purpose of this paper is to ascertain what diagnostic aid may be obtained from the characteristics of pathologic serous body fluids as demonstrated by easily performed tests.

Although paracenteses were practiced as early as the time of Hippocrates, the study of the fluid thereby obtained has been going on for only a century. One of the earliest investigations of the chemical constituents was that of Marcet¹ in 1811, when paracentesis was still a doubtful procedure. A quarter of a century later Guérin² declared that the practice of thoracentesis must continue, despite the small number of successes, since it offered the only hope of recovery. The first major work on the cellular constituents was done by Widal and Ravaut³ in 1900.

MATERIAL

From the case records chiefly of the Peter Bent Brigham Hospital, but also of the Boston City, Beth Israel and Children's hospitals, data recorded on over 1300 fluids were collected and classified; only those in which there was no reasonable doubt as to the diagnosis were accepted. The technique employed in carrying out the various tests was basically uniform, even though some had been performed as long as twenty-five years previously.

OBSERVATIONS

Specific Gravity

It is commonly stated in the current textbooks on clinical pathology that the dividing line between infected and noninfected fluids occurs at the specific gravity of 1.016, although little experimental work to support this statement could be found

in the literature. Reuss⁴ in 1881 and Runeberg⁵ in 1884 did some work on this subject, but they emphasized the relation of the specific gravity to the protein content. The results of an attempt

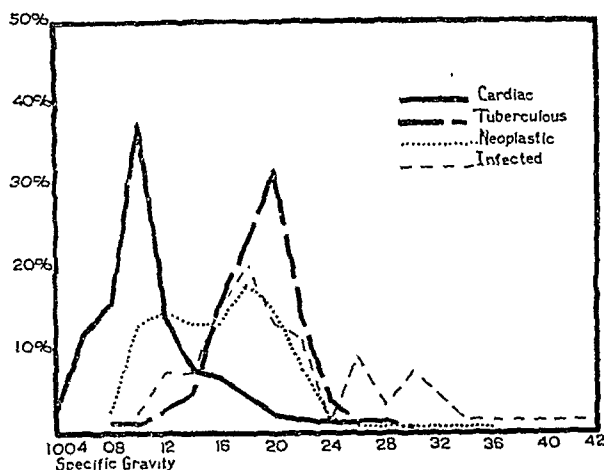


FIGURE 1. The Distribution of the Specific Gravities of 313 Cardiac, 290 Tuberculous, 123 Neoplastic and 100 Infected Pleural Effusions.

at differentiation on this basis can be seen in Figures 1 and 2, where 863 pleural and 468 peritoneal effusions are compared. From the pleural cavity,

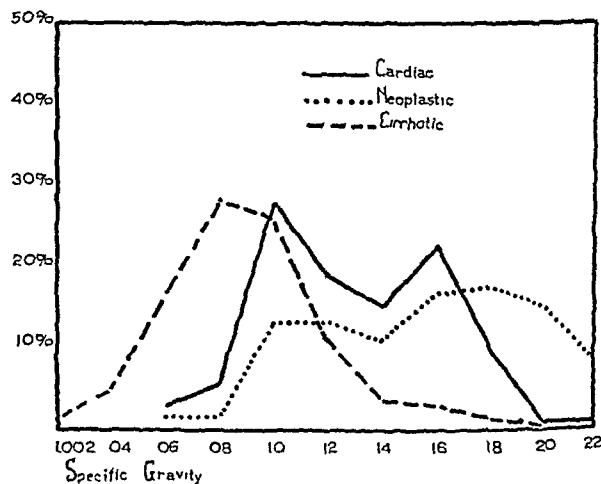


FIGURE 2. The Distribution of the Specific Gravities of 100 Cardiac, 60 Neoplastic and 270 Cirrhotic Peritoneal Effusions.

313 cardiac fluids showed an average specific gravity of 1.010, with 10 per cent 1.016 or more; 290 tuberculous fluids showed an average specific gravity of 1.020, with 10 per cent 1.016 or less; 100 effusions associated with pulmonary infection av-

*From the Medical Clinic, Peter Bent Brigham Hospital.

†Formerly, assistant resident in medicine, Peter Bent Brigham Hospital; now, of Pittsfield, Massachusetts.

eraged 1019, with a range of 1010 to 1042, 123 neoplastic fluids showed no peak, but a plateau ranging from 1010 to 1020, 21 cirrhotic effusions averaged 1010, with a range of 1004 to 1019; and 16 nephrotic fluids averaged 1006 with a range of 1001 to 1008. From the peritoneal cavity, 270 cirrhotic fluids showed an average specific gravity of 1009, 60 neoplastic effusions showed a plateau of 1010 to 1020; 21 tuberculous fluids averaged 1020, 17 nephrotic fluids averaged 1007, with a range of 1003 to 1012; and 100 cardiac effusions

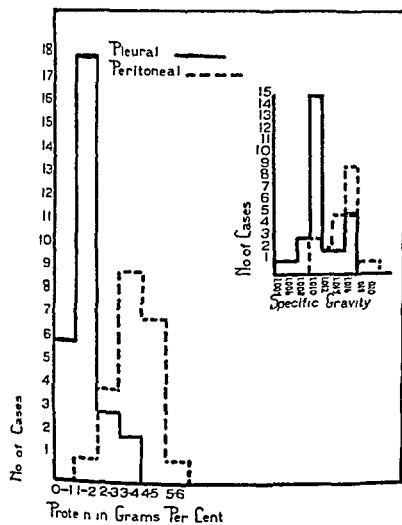


FIGURE 3 The Distribution of Protein Levels and Specific Gravities in Cardiac Fluids

averaged higher than those from the pleural cavity, 34 per cent having a specific gravity of 1016 or more. A similar discrepancy between the cardiac pleural and peritoneal fluids was found in the protein content (Fig 3). No explanation for this was found on reviewing the case records.

Of the cardiac pleural fluids, approximately 75 per cent were withdrawn from the right chest cavity, a phenomenon for which several explanations have been offered.⁶ Cirrhotic and nephrotic effusions are usually of low specific gravity, probably because the mechanism involved in their formation depends on lowered blood-colloid osmotic pressure rather than on increased venous pressure or increased capillary permeability.

The determination of the specific gravity is liable to many errors. As can be readily found in textbooks of physical chemistry, the specific grav-

ity of solutions is markedly affected by temperature. In simple experiments using the ordinary laboratory hydrometer (urinometer), it can be shown that raising a serous fluid from room to body temperature may decrease its specific gravity by as much as 0.008 to 0.010. The common hydrometers now on the market are corrected for a temperature of 60°F (15.5°C), a level of temperature that is rarely found in the routine laboratory. Even when the specific gravity of a serous fluid is determined by weight, a similar change is noticed.⁷ In the above tabulations, it is probable that most of the fluids were studied at or near the usual room temperature of 70°F and therefore showed a specific gravity slightly lower than that actually present. This error was essentially constant throughout. (The specific gravity determinations on urine are of course subject to the same error⁸.) In both transudates and exudates the clot, which usually forms after the fluid has been standing for an hour or two, has almost no effect on the specific gravity.⁷ Abnormal lipid content is said to have

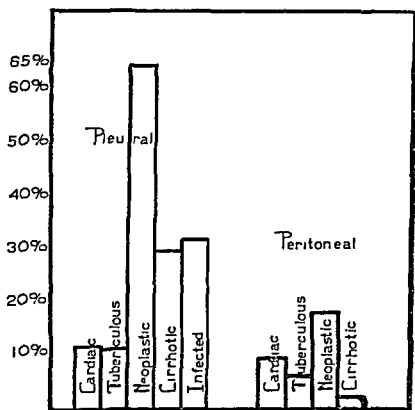


FIGURE 4 The Percentage of Various Types of Effusions with a Red Blood Cell Count of 10,000 or More

These figures are based on observations in 274 cardiac, 164 tuberculous, 100 neoplastic, 13 cirrhotic and 59 infected pleural fluids and 46 cardiac, 15 tuberculous, 49 neoplastic and 135 cirrhotic peritoneal fluids.

little effect on the specific gravity, at least in the plasma.⁹ Lowering of the blood protein undoubtedly plays some part in lowering the protein content of effusions.

Cellular Constituents

Another examination commonly made of these fluids is that of the total number and percentage composition of the various blood cells. Observa-

tions in 611 pleural and 245 peritoneal fluids showed that bloody or blood-tinged fluids, that is, those containing 10,000 or more red blood cells per cubic millimeter, were not strikingly characteristic of any of the specific types except the neoplastic (Fig. 4). A red-cell count of 10,000 or more was found in 65 per cent of neoplastic fluids, 31 per cent of fluids associated with pulmonary infection, 30 per cent of cirrhotic fluids, 11 per cent of cardiac fluids and 10 per cent of tuberculous fluids in the pleural cavity; in the peritoneal cavity this red-cell count was found in 20 per cent of neoplastic, 10 per cent of cardiac, 7 per cent of tuberculous and 1 per cent of cirrhotic effusions. The trauma incidental to the paracentesis may play a part in elevating the red-cell count, since the leakage of but 2 cc. of normal blood into 1000 cc. of fluid would give a count of 10,000. In the nontraumatic pleural fluids, a marked elevation of the red-cell count, that is, above 100,000, was excessively rare except in neoplastic fluids, where it occurred in 12 per cent of the cases. Only 1 per cent of the cardiac pleural fluids had such a large number of erythrocytes. Contrary to the common opinion, bloodiness in tuberculous effusions is unusual. That the occurrence of blood in significant amounts is much less common in peritoneal fluids than in those from the pleura is probably explained by the greater volume of fluid in the former, which causes a greater dilution of whatever blood may flow into it. Even markedly hemorrhagic effusions may not exhibit frank blood clots unless they have been withdrawn soon after the bleeding has taken place. Denny and Minot¹⁰ have shown that this is due to intrapleural clotting and defibrination, rather than to any specific anticoagulant.

The total and differential white-cell counts have been studied by many investigators.¹¹⁻¹³ In an analysis of 759 pleural and 389 peritoneal effusions, the count was found to be above 1000 in the pleural cavity in 85 per cent of fluids associated with pulmonary infection, and 73 per cent of tuberculous, 42 per cent of neoplastic, 27 per cent of cirrhotic and 10 per cent of cardiac fluids; in the peritoneal cavity such an elevation was found in 76 per cent of tuberculous, 51 per cent of neoplastic, 11 per cent of cirrhotic and 10 per cent of cardiac effusions (Fig. 5).

The differential white-cell count is of little value in the individual case, with the exception of non-tuberculous infected fluids, where a polymorphonuclear leukocytosis is the rule. In 229 tuberculous pleural fluids, there were 9 proved cases in which the polymorphonuclear cells constituted 50 per cent or more of the total count. According to experimental work, such a neutrophilia may appear

early in the disease.¹⁴ In 13 of 232 cardiac pleural fluids, in 21 of 198 cirrhotic peritoneal fluids and in an occasional neoplastic effusion, the total white-cell count consisted of more than 50 per cent polymorphonuclear cells, even though no infection was

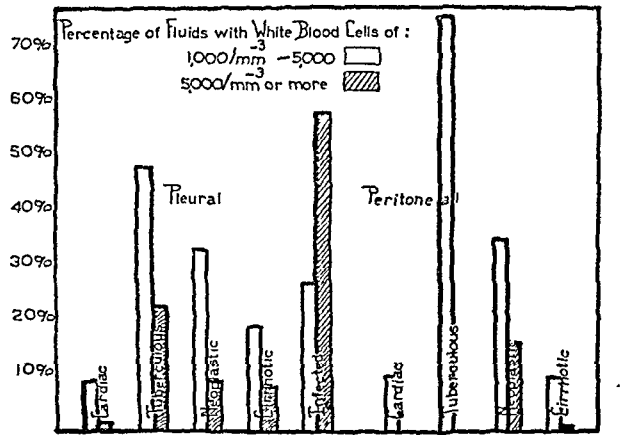


FIGURE 5. The Percentage of Various Types of Effusions with a White-Blood-Cell Count of 1000 or More. These figures are based on observations in 278 cardiac, 250 tuberculous, 104 neoplastic, 26 cirrhotic and 101 infected pleural fluids and 69 cardiac, 13 tuberculous, 51 neoplastic and 256 cirrhotic peritoneal fluids.

present. Neoplastic cells have been identified in effusions with varying results, and no fixed criteria for their recognition have been accepted.¹⁵

Chemical Constituents

Determinations of the protein content of the various types of effusions have been made by numerous investigators.^{11, 13, 16-19} Table 1, which

TABLE 1. Protein Content of Different Types of Effusions.

TYPE OF FLUID	NO. OF CASES	PLEURAL PROTEIN		NO. OF CASES	PERITONEAL PROTEIN	
		AVERAGE	RANGE		AVERAGE	RANGE
		gm. per 100 cc.	gm. per 100 cc.		gm. per 100 cc.	gm. per 100 cc.
Cardiac	29	1.6	0.2-3.6	21	3.7	1.5-5.3
Tuberculous	3	4.2	2.7-5.1	0		
Neoplastic	9	3.4	2.1-4.6	15	3.2	1.5-4.2
Cirrhotic	5	1.8	0.6-3.2	69	1.2	0.6-3.2
Nephrotic	10	0.4	0.1-1.0	9	0.3	0.1-0.9

summarizes 170 protein determinations, shows that there may be wide variation, so that no absolute differentiation of the various types is possible on this basis. In the literature^{11, 20, 21} there is considerable disagreement as to whether the protein content of a serous fluid bears any such frank relation to its specific gravity as has been shown in the blood²² and lymph.⁹ A rough relation is apparent in Figure 3. Investigations showing that such a relation does exist have been completed, and are to be reported.⁷

The protein content of transudates tends to rise with resorption; that of exudates may vary in

either direction but usually is lower.²³⁻²⁷ Such factors undoubtedly account at least in part for the wide range of the protein concentration. Yamada²⁸ found in a large series of cases that pleural fluid obtained from normal persons contained an average of 1.77 gm. of protein per 100 cc., with a range of 1.38 to 3.35. The albumin-globulin ratio tends in general to be like that of the blood, so that it is most commonly found reversed in cirrhotic effusions. The effect of clotting on the protein content of the fluids is slight.

Other chemical constituents of pathologic fluids have not been significant in determining the cause of the effusion. Readily diffusible substances, such as bilirubin, nonprotein nitrogen substances and sugar, are in essentially the same concentration as they are in the blood, and ionized substances, which are subject at least in part to Donnan's equilibrium, appear at different levels. Total fats are usually quite low. The cholesterol content may occasionally show a considerable elevation without any frank relation to the blood content; it has a tendency to be elevated in neoplastic disease.²⁹

Unusual Fluids

The finding of a *milky* or *chylous fluid* on paracentesis has proved sufficiently unusual to bring about the careful study of a number of samples.³⁰ An effusion should not be diagnosed as chylous unless a thin layer of it has a white opacity, like milk, since a certain degree of haziness or opacity is common in transudates, particularly in those associated with cirrhosis and nephrosis. In general, the chylous fluids have been divided into those associated with obvious thoracic-duct obstruction and those where no such lesion was found. Since these two types cannot be differentiated by ordinary laboratory methods, such a division seems worthless for the clinician, particularly because rupture of the thoracic duct has repeatedly been demonstrated to be an inconstant cause of such fluids because of collateral circulation.^{31, 32} Occasionally the milkiness has been found to be due not to an ordinary fatty material but to a lecithin-globulin complex.³³ In cases unassociated with obvious traumatic rupture of the thoracic duct, the commonest causes of milky fluid in order of decreasing frequency are neoplasm, tuberculosis, nephrosis and cirrhosis. Among the 12 cases encountered with chylous fluids the underlying disease was cirrhosis (5 cases), neoplasm (3 cases), nephrosis (2 cases) and subacute bacterial endocarditis (1 case); in 1 case, that of a child, it was associated with volvulus.³⁴ In 1 of the cases where cirrhosis was proved at autopsy, variation in the dietary intake of fat had no effect on the degree of

miliness, which decreased with consecutive paracenteses. The diagnosis of chylous effusion may occasionally be made on x-ray examination, since the fluid, owing to its unusually high fat content, does not hinder to any extent the passage of the rays as do other effusions.³⁵

Eosinophilic fluid is discussed periodically in the literature, with no definite conclusion as to its etiology.³⁶ In at least two thirds of the cases the fluid is also bloody, a finding perhaps related to that of Cunningham,³⁷ who discovered the most pronounced eosinophilia in those cases of chronic pleurisy artificially induced by washed or laked red cells. The wide number of reported underlying diseases suggests a complete lack of specificity of this finding. In the 14 eosinophilic fluids found during these investigations, all but 3 were bloody. Six of them were apparently due to a benign pleurisy of unknown cause in which guinea-pig inoculations proved negative for tuberculosis; 4 were associated with neoplasm, 2 with cardiac decompensation (after repeated taps) and 2 with empyema. Only occasionally did the circulating blood show an eosinophilia. In this connection it may be added that Charcot-Leyden crystals have occasionally been reported in effusions.³⁸ In but 1 of all the cases here collected was such a finding reported, the diagnosis being cardiac decompensation.

On the subject of *cholesterol effusions* the reports in the literature are in close agreement.³⁹ The fluid, described as being filled with golden, glittering particles, is shown microscopically to consist of characteristic cholesterol crystals in suspension. Almost all the fluids reported had been found years after a spontaneous untreated pleurisy, peritonitis or pericarditis, and in some, tubercle bacilli were demonstrated. Only one doubtful example was found in the cases reviewed here.

Mucinous effusions, particularly from the peritoneal cavity, are occasionally reported in the literature and are apparently always associated with neoplasm.^{40, 41} In this series, 2 such fluids were found. In one, a case of peritoneal carcinomatosis, the abdominal fluid, described as glairy, had a specific gravity of 1.010 with a total protein content of 2.5 gm. per 100 cc. The other case, that of a patient apparently suffering from carcinoma of the ovary metastatic to the peritoneum and pleura, had mucinous fluid in both cavities; the fluids had a specific gravity of 1.018 and a protein content of 4.5 gm. per 100 cc.

Rheumatic effusions, which occur in a small fraction of cases of acute rheumatic fever, exhibit many of the properties commonly ascribed to exudates with a relatively high specific gravity, a tendency to bloodiness, and rapid clotting thought to

be due to a high fibrin content.⁴² In the 9 cases studied at the Peter Bent Brigham Hospital, no comment was made of rapid clotting. In the 8 cases in which the specific gravity was noted, 4 were 1.017 or more. The white-cell count ranged from 370 to 33,600 and the red-cell count from 77 to 45,000.

A review of the literature on the characteristics of *pericardial fluids* reveals that very little investigation has been done. Although the amount of fluid normally found in the pericardial sac surpasses that found in the pleural and peritoneal cavities, only four references could be found to protein determinations of normal pericardial fluid, and all were done before the development of modern chemical methods. The fluid in tuberculous pericarditis is usually of a high specific gravity and is more frequently sanguineous than the fluid of a tuberculous pleurisy, according to the literature.^{43, 44} In 3 cases of tuberculous pericardial effusion examined in this series, the specific gravity was 1.018 or more in all, with the red-cell count exceeding 10,000 in all but one of 7 specimens examined. Bloody pericardial fluid may be found in a variety of conditions, including rupture of the coronary vessels, tumors of the heart and pericardium, chronic nephritis and nontuberculous pericardial infections.⁴⁴ Clotting of these fluids occurs only when they are withdrawn shortly after their appearance. Even when chylous pleuritic and peritoneal fluids are present, chylopericardium is very rare. Only 3 cases have been reported.³⁰ Occasional cases of cholesterol pericarditis have been seen.⁴⁵

SUMMARY AND CONCLUSIONS

The customary division of transudates from exudates at the specific gravity of 1.016 has been found to be true only in certain diseases. Thus in pleural effusions, 90 per cent of cardiac fluids have a specific gravity of 1.016 or less, and 90 per cent of tuberculous fluids have a specific gravity of 1.016 or more. In ascites, 95 per cent of cirrhotic effusions are in the transudative range, and no cases of tuberculous peritonitis were found in which the specific gravity was considered typical of transudates. In nontuberculous infected pleural fluids, on the other hand, 31 per cent are of specific gravity 1.016 or less, and 34 per cent of cardiac peritoneal effusions have a specific gravity of 1.016 or more.

Neoplastic fluids from both the pleural and peritoneal cavities are about evenly divided between the exudative and transudative specific gravities.

Nephrotic fluids have a uniformly low specific gravity in the pleural and peritoneal cavities.

The specific gravity of cardiac peritoneal fluids is usually higher than that of cardiac pleural fluids.

The chief cause of error in the determination of specific gravity is the temperature of the fluid, which may change the specific gravity by as much as 0.008 to 0.010.

The etiology and characteristics of 12 chylous, 14 eosinophilic, 2 mucinous and 8 rheumatic effusions from the pleural and peritoneal cavities and 3 tuberculous effusions from the pericardial cavity, are presented.

Bloody or blood-tinged fluids from both the pleural and peritoneal cavities are predominantly neoplastic in origin. Tuberculous, nontuberculous infected, cirrhotic and cardiac effusions are responsible for a small percentage.

The total white-cell count is above 1000 per cubic millimeter three times as frequently in infected as in noninfected fluids from both the pleural and peritoneal cavities. Neoplastic fluids have a white-cell count above 1000 in 50 per cent of the cases.

The protein content of effusions contributes no more than does the specific gravity to the diagnosis.

The differential white-cell count is of little diagnostic value except in differentiating nontuberculous infections.

REFERENCES

1. Marcer, A.: A chemical account of various dropsical fluids. *Med.-Chir. Tr.* 2:342-384, 1817.
2. Guérin, P. B. J.: Sur le traitement de la pneumonie et de la pleurésie aiguës. *Paris thésis.* No. 29, 1838. Pp. 1-26.
3. Vidal, P., and Ravaut, P.: Applications cliniques de l'étude histologique des épanchements séro-fibrineux de la plèvre (pleurésies infectieuses aiguës). *Compt. rend. Soc. de biol.* 52:653-655, 1900.
4. Reuss, A.: Das Verhältniss des specifischen Gewichts zum Eiweissgehalt in serösen Flüssigkeiten. *Deutsches Arch. f. Klin. Med.* 28:317-322, 1881.
5. Runeberg, J. W.: Klinische Studien über Transsudationsprocesse im Organismus. *Deutsches Arch. f. klin. Med.* 35:266-300, 1884.
6. Dock, W.: The anatomical and hydrostatic basis of orthopnea and of right hydrothorax in cardiac failure. *Am. Heart J.* 10:1047-1055, 1935.
7. Paddock, F. K.: The relationship between the specific gravity and the protein content in human serous effusions. *Am. J. M. Sc.* (in press).
8. Windsor-McLean, L. A.: The temperature as a factor to be considered in clinical urinalysis. *M. J. Australia* 2:467-470, 1938.
9. Weech, A. A.; Reeves, E. B., and Goettsch, E.: The relationship between the specific gravity and the protein content in plasma, serum, and transudates from dogs. *J. Biol. Chem.* 113:167-174, 1936.
10. Denny, G. P., and Minot, G. R.: The coagulation of blood in the pleural cavity. *Am. J. Physiol.* 39:455-458, 1916.
11. Foord, A. G.; Youngberg, G. E., and Wetmore, V.: The chemistry and cytology of serous fluids. *J. Lab. & Clin. Med.* 14:417-428, 1929.
12. Scott, T. F. M., and Finland, M.: The cytology of pleural effusions in pneumonia studied with a supravital technique. *Am. J. M. Sc.* 188:322-332, 1934.
13. Joly, F.: Cyto-diagnostic et albumino-diagnostic dans les épanchements pleuraux des cardiaques. *Paris méd.* 1:423-428, 1935.
14. Montgomery, L. G., and Lemon, W. S.: The cellular reaction of the pleura to infection with *Mycobacterium tuberculosis*. *J. Thoracic Surg.* 2:429-438, 1933.
15. Schlesinger, M. J.: Carcinoma cells in thoracic and in abdominal fluids. *Arch. Path.* 28:283-297, 1939.
16. Schade, H.; Clausen, F.; Häbler, C.; Hoff, F.; Mochizucki, N., and Birner, M.: Weitere Untersuchungen zur Molekularpathologie des Entzündung: Die Exsudate. *Ztschr. f. d. ges. exper. Med.* 49:334-410, 1926.
17. Kylin, E.: Studien über den colloidosmotischen Druck: der colloidosmotische Druck des Blutes und Pleuraexsudat bei Pleuritis exsudativa. *Acta med. Scandinav.* 72:561-570, 1929.
18. Reiche, F.: Die chemische Zusammensetzung tuberkulöser Pleuraexsudate und anderer Ergüsse in die Brusthöhle. *Beitr. z. Klin. d. Tuberk.* 74:652-662, 1930.
19. Takahashi, R.: Untersuchungen über die chemischen Eigenschaften des Pneumokokkenempyem-Eiters: chemische Analyse des Pneumokokkenempyem-Eiters. *Orient. J. Dis. Infantis* 11:1-4, 1932.

treated by his method, although Hollander⁴ has recently reported successful treatment in a small series of patients with severe pruritus ani by tattooing the involved perianal skin with cinnabar (mercuric sulfide), and Manheim,⁵ after using a similar technic, has confirmed the immediate success of this method.

An obvious factor, which is constantly present and is mentioned only casually by all authors, is that of anal hygiene and cleanliness. Contamination of the anus and perianal skin by feces after defecation is constantly present in all patients, and is also the one factor that persists after medical, physical or surgical treatment of pruritus ani.

Tucker and Hellwig⁶ in a very significant study emphasized the importance of feces in pruritus ani. They studied specimens removed at biopsy from 43 cases in various stages of the disease and classified associated skin lesions in four degrees of severity, that is, exudative inflammation, epidermoid proliferation, atrophy of the epidermis and sebaceous glands, and epithelial defects. These authors comment on the similarity of the histologic picture seen in the first two stages of pruritus ani and the pathologic lesions of the skin in cases of chemical dermatitis. They state that the "hydrops of the epidermis cells, irregular proliferation of the stratum mucosum and of the hair follicles, hyperkeratosis with plugging of the hair follicles and atrophy of the sebaceous glands [seen in pruritus ani], are changes characteristic of dermatitis due to chemical irritants." Of the 43 cases examined by them, none showed changes attributable to allergy or neurogenic factors. Furthermore, biopsied specimens from the anal canals showed no pathologic lesions and were similar in appearance to the histologic picture of specimens from the anal canal in 343 patients without pruritus ani. Tucker and Hellwig argue from this that though anal and rectal disease may exist in patients with pruritus ani, the anal lesion per se is not the essential cause of the pruritus. They conclude that pruritus ani seems to be a simple chemical dermatitis due to "something" in the feces, and suggest as the irritant skatole or some similar decomposition products of proteins. This theory is well in accord with the clinical experience of all observers. With careful anal cleanliness, that is, keeping the perianal skin free of feces, most patients with mild pruritus ani can keep free of symptoms.

According to Caskey,⁷ a number of patients present themselves with lesions of the perianal skin that are definite dermatologic entities. The most frequent of these conditions are the mycotic lesions evidenced by a sodden epidermal circle extend-

ing outward from the anus and often upward between the gluteal folds. Because of secondary bacterial contamination, it is extremely difficult to culture the fungus. Castellani,⁸ in a carefully studied series of patients with pruritus ani extending over thirteen years, was able to demonstrate epidermophytosis in 20 per cent. Terrell and Shaw⁹ report similar results. Patients with perianal skin lesions due to fungous infections frequently have associated mycotic interdigital lesions, tinea cruris of the groin or phytid eczematoid lesions on the hands. Lichen planus can occur in the perianal region, and is distinguished by violaceous patches made up of smaller individual polyangular flat-topped lesions with little or no pruritus. One such case was treated unsuccessfully by injections and this was followed by hemorrhoidectomy, presumably for pruritus ani. The perianal lesions of lichen planus yield promptly to roentgen-ray therapy.

Psoriasis occasionally occurs in the perianal region and presents a sodden beefy appearance. In these cases diagnosis is clarified by typical psoriatic lesions elsewhere. Circumscribed neurodermatitis may appear in the anal region, and is characterized by a dry lichenified infiltrated lesion. It is highly resistant to treatment, as is evidenced by a patient in this series who was treated by devious therapeutic measures for three years with no constant remission. Oxyuris (pinworms), a competent cause of anal itching, is seen most frequently in children but occasionally in adults. In this series, oxyuris was the etiologic factor in 1 adult patient, who was treated successfully with hexylresorcinol administered orally and by enemas.

Many authors associate idiopathic pruritus ani with the psychoneuroses. This relation is suggested in the psychoanalytic material of a case reported by Saul,¹⁰ who states: "He occasionally indulged in anal masturbation and stated that he often used pruritus merely as an excuse for his indulgence. The regular recurrence of pruritus when his passive homosexuality was aroused, as well as the analytic material, left no doubt as to the connection. It is of interest that the pruritus was often relieved by a satisfactory defecation." Increasing interest in psychosomatic medicine should make us heedful of pruritus ani as a major symptom in obvious psychoneurotics, and in such patients psychotherapy is indicated if simple medical or surgical treatment fails.

To recapitulate, it seems that physicians do not treat pruritus ani from the etiologic aspect but direct their therapy to the symptom. This is accomplished chiefly by the following means: nerve block—anesthetic ointments, subcutaneous injec-

tion of oil-soluble anesthetics, quinine compounds, distilled water, hydrochloric acid and alcohol, undercutting operations and roentgen-ray therapy; excision of anal lesions—internal and external hemorrhoids and skin tags, crypts and papillae, and fissures and fistulas; and biological and chemical therapy—vaccines and tattoo with cinnabar. Such secondary measures as dietary restrictions for possible allergy, general sedatives and anal hygiene are mentioned by most writers.

There is, therefore, no universally adequate treatment for pruritus ani, inasmuch as no common etiology has been accepted. My experience with varied forms of treatment has been that recurrences are frequent, and that occasionally severe complications occur after certain therapeutic measures. Two patients developed perianal abscesses following subcutaneous injection of anesthetic oil solutions, and a severe abscess followed alcohol injection by the Stone technic. These cases required extensive surgical procedures, and convalescence was protracted. Huhner¹¹ reports 6 cases of azoospermia following roentgen-ray treatment administered by competent dermatologists for dermatoses of the perineal region. Four of these were known to have had active spermatozoa before treatment. The testicles had evidently been protected, but insufficiently. I have had a similar case. These experiences warn against the use of roentgen ray in the treatment of pruritus ani in fertile men.

As stated, despite the specific measures outlined above, one constant factor is present in all cases of pruritus ani, namely, soiling of the perianal skin with feces. It is probable that in certain atopic patients sensitivity to chemical substances in their own feces by constant contact results in perianal dermatitis, with itching as the chief symptom. Furthermore, the perianal skin is naturally well adapted as a medium for the development of a contact dermatitis, since heat, moisture, skin folds, perspiration and hair are all present. Added to mechanical friction on walking or sitting is the act of using toilet tissue after defecation. This is really tantamount to anointing feces into the perianal skin. Feces contain numerous chemical substances that can act as irritants to the skin. Among these are the bacteria and their exotoxins, intestinal enzymes and even the end results of bacterial action on proteins—the indoles, phenols and skatole. Furthermore, I¹² have shown that indole, skatole and fecal emulsions will produce a dermatitis when applied as a patch test in sensitive persons.

Inflammatory lesions in the anal canal and lower rectum, proctitis, hypertrophied papilla, in-

fectected anal crypts, mucosal fissuration, chronic fistula or anal fissure may cause anal pruritus. This results in maceration of the perianal skin by constant soiling with irritating pus and by actual inflammatory changes in the sensory end nerves in hypertrophied papillae and perianal skin. As Scarborough¹ and others have shown, anal lesions must be treated surgically to ensure elimination of such obvious causes of pruritus. Scarborough found local pathologic lesions present in all of 152 cases of pruritus ani. Fifty-two of these were satisfactorily treated by surgical measures, and in this group pruritus did not recur, a perfect result. It must be emphasized, however, as stated by this author, that these findings were reported shortly after operation, and that some late recurrences may be expected.

Perianal skin lesions frequently seen associated with pruritus are due primarily to mechanical abrasions caused by irresistible scratching and subsequent infection. In many patients this is subconscious, occurring during sleep, frequently awakening the patient and preventing further sleep. Occasionally well-defined cellulitis results from this form of induced infection, complicating the treatment of the essential pruritus. Furthermore, this inflammatory skin lesion may be a contributory factor in perianal abscesses occasionally resulting from the subcutaneous injection of alcohol or anesthetic oil.

The concept that patients with obstinate pruritus ani are specifically sensitive to a chemical substance or substances occurring in feces forms the basis of treatment in this report. I believe that this relation exists and is an important causative factor of pruritus in all sensitive cases except those due to mycotic or other specific dermatologic entities. Obviously surgical conditions such as anal ulcer, fissures, fistulas and cryptitis are excepted, as are cases of oxyuris infestation. Excepted also is the occasional patient with a psychoneurotic anal fixation, in whom pruritus ani is a symptom.

In this series a detailed history was obtained especially with regard to previous treatment and length of remission following treatment. General physical examinations, urine analyses and blood serological tests were routinely performed. On rectal examination, inspection of the anal region was considered to be important. Skin lesions were classified arbitrarily on inspection in degrees from normal to third, depending on the severity of the dermatitis. The patient was asked to strain or bear down in order to determine the possible presence of prolapsed mucosa. Careful digital examination demonstrated sphincter tone and palpable pathologic lesions, such as hypertrophied papillae, fissures and

polyps. Sigmoidoscopy was routinely performed to rule out the possibility of lesions high in the rectum and sigmoid. Anoscopic examination is essential. In many patients, the rectal mucosa prolapses into the lumen of the examining instrument. Mucosal prolapse is a vital causative factor in soiling the perianal skin because with sitting, coughing, straining or passing flatus a prolapsing mucosa

TABLE 1. Data on 100 Patients Referred for Treatment of Severe Pruritus Ani.

DATA	No. OF CASES
Sex	
Male	60
Female	40
Duration	
Less than 6 mo	8
6 to 12 mo	16
1 to 3 yr	33
3 to 6 yr	18
6 to 10 yr	8
10 to 15 yr	7
Over 15 yr	10
History	
Worse at night	73
Worse before or after defecation	43
Specific food allergy	9
Previous therapy	
Local medication only	76
X ray	15
Subcutaneous nerve block injections, alcohol, anesthetics etc	19
Undercutting operations	4
Hemorrhoidectomy	8
Surgery for fissure	4
Perianal dermatoses	
Absent	17
Present	83
1st degree (mild)	28
2nd degree (moderate)	36
3rd degree (severe)	19
Anorectal lesions	
Absent or insignificant	18
Excess skin tags	15
Prolapse of mucosa	42
Moderate or large internal hemorrhoids	27
Hypertrophied papillae	25
Fissure on anal mucoderm	12
Inflamed crypts	12
Granular proctitis	13
Fissure in ano	3
Disposition	
Did not return	11
Anal hygiene regimen only	50
Referred for surgical therapy of anorectal lesions	21
Refused surgery, did not return	9
Surgery, followed by anal hygiene	12
Sclerotic injection for internal hemorrhoid or mucosal prolapse, anal hygiene	16
Psychotherapy	4

can extrude rectal mucus or feces through the anal sphincter. Many patients had residual feces in the lower rectum despite the fact that defecation had occurred shortly before examination. This is significant in the causation of pruritus, because many patients have learned by experience that an attack of pruritus can be temporarily abated by a cleansing rectal lavage. Similarly, the presence of large internal hemorrhoids contributes to perianal soiling by partial prolapse through the anus.

Treatment is directed mainly toward keeping the perianal skin free of feces. As pointed out,

gross pathologic lesions, redundant rectal mucosa, prolapsing hemorrhoids and hypertrophied papillae favor perianal soiling and must be eliminated by surgery. Secondary skin infections, such as cellulitis, skin and mucosal fissures and abrasions from scratching, must be treated by measures directed toward restitution of a fairly healthy skin. Obvious surgical lesions such as anal ulcer and fistulas, which soil the skin with irritating pus, must be adequately excised.

Table 1 gives an analysis of one hundred patients with pruritus ani seen in the proctological clinics of the New York and French hospitals. The material varied from relatively mild cases of short duration to very severe, almost intractable lesions.

In the routine treatment of these cases it is explained to the patient that there is a direct relation between perianal soiling with feces and the itching. Furthermore, it is emphasized that successful treatment depends on the patient's careful co-operation in following instructions, and responsibility for success or failure of treatment is thereby placed squarely on him. Instructions in the care of the perianal region are carefully explained, and the following written directions are given to him:

After defecation whenever possible take a rectal enema, using a pint of plain warm tap water. Expel this immediately. A convenient method is through the use of a rubber hand syringe. Cleanse the perianal skin with wet absorbent cotton. Do not use toilet tissue. Dry well with cotton and powder well with cornstarch or talcum. Cleansing with wet cotton and dusting with powder must be repeated about four times daily, depending on the amount of moisture and the degree of itching. Always keep the skin around anus clean and dry. Carry cotton and talcum in separate envelopes on the person in a pocket or handbag. Before retiring repeat rectal lavage, and cleanse, dry and powder the anal region. After retiring rub a small amount of ointment well into the perianal skin. This may cause burning for several minutes.

Rectal lavage is directed toward removing residual feces from the lower rectum and anus after defecation and is advised before retiring, because in many patients the itch is intensified at night. Through the day feces may accumulate in the lower rectum, and their removal before retiring frequently prevents nocturnal itching. Mineral oil is interdicted in our patients because we have found that oil stained with feces frequently leaks through the anus to soil the perianal skin.

Half-strength Whitfield's ointment is used routinely:

Salicylic acid	1.0 gm.
Benzoic acid	2.0 gm.
Petrolatum	300 gm.

This can be modified by adding a small quantity of menthol. This preparation is used for two reasons. In the first place, mycotic infections, primary or secondary, are associated with pruritus ani in about 20 per cent of all patients (Castellani⁸), although it is difficult to demonstrate the specific fungus. It is advisable therefore, to employ empirically an antimycotic medication such as Whitfield's ointment. Secondly, this ointment applied to the perianal skin causes moderately severe burning for about ten minutes. This burning is accepted subjectively as far more satisfactory than the usual intolerable itching that plagues the patient after retiring, and, in addition, the necessity for scratching is removed. Further abrasions and reinfection of the perianal skin are thus prevented, the vicious circle is broken, and the excoriated and infected skin tends to heal rapidly.

Patients with second-degree or third-degree perianal lesions, that is those with edematous, inflamed and excoriated skin, and those with localized cellulitis, are treated with applications of wet dressings. The dressings are applied overnight by means of a perineal pad under a T binder; in very severe cases, bed rest for several days, with constant wet dressings, is advised. Hamamelis and tap water are utilized. Treatment with ointment is withheld until the condition of the skin has improved, but rectal lavage and perianal cleansing are used as described.

Associated pathologic lesions in the lower rectum and anus are treated surgically, either by op-

of the patients soon after cessation of treatment or because of careless treatment.

Follow-up data were secured at re-examination from six to twelve months after the first visit. The results of this routine treatment are based on the report of patients as to their subjective symptoms, that is, itching, exudate, burning and pain. Of 100 patients, 20 did not return after the first visit, or refused surgery for anorectal lesions. Of the remaining 80 patients, 20 per cent reported fair improvement after several weeks under routine management, and 73 per cent reported excellent results, a total of 93 per cent in whom management by this means resulted satisfactorily. The best results were obtained in the more co-operative patients regardless of the amount of skin change or the duration of the disease. Of 50 patients who were followed after six months, forty (80 per cent) reported recurrence of pruritus on cessation of treatment, or after an interval of careless treatment. Only 10 patients remained well. These figures confirm the relation of perianal soiling with feces to pruritus ani.

SUMMARY

Pruritus ani is a symptom resulting from numerous causes, some of them obscure. Obvious causes are dermatologic entities, that is, mycotic infections, neurodermatitis, lichen planus, psoriasis, oxyuris infestations and psychoneurosis with anal fixation. Pathologic lesions in the lower rectum or anus are responsible wholly or in part for pruritus ani. Among these are redundant prolapsing rectal mucosa, internal hemorrhoids, proctitis, hypertrophied papillae, cryptitis, fissures and fistulas. These conditions when found must be eliminated surgically. The concept of pruritus ani as a reflex symptom due to disease in a distant organ is untenable, because it is not supported by satisfactory clinical evidence.

In many cases there appears to be a direct relation between fecal soiling of the perianal skin and the presence of pruritus ani. This is evidenced as a dermatosis induced in the perianal skin by irritant substances in the feces of specifically sensitive (atopic) patients. Evidence favoring this concept exists in studies of the involved skin, which show changes similar to those found in other types of chemical dermatoses. Positive patch-test reactions to solutions of indole, skatole and fecal emulsions obtained in some patients with active pruritus ani are further evidence in regard to etiology. It seems likely that constant soiling of the perianal skin with feces is responsible for the recurrences which are so frequent after symptomatic treatment, such as sensory-nerve block by injections

TABLE 2. *Results of Therapy.*

RESULT	NO. OF CASES	PER CENT
Follow-up 2 months or less		
Failure	3	4
Poor	2	3
Good	16	20
Excellent	59	73
Total	80	
Follow-up 6 months or more		
Well	10	20
Recurrence with careless treatment	26	52
Recurrence with cessation of treatment	14	28
Total	50	

eration or by injection of sclerosing solutions when indicated in cases of redundant mucosa or internal hemorrhoids. Treatment with anal hygiene, lavage and ointment is utilized throughout the period of surgical therapy and maintained thereafter.

It has been our experience that with clinical improvement patients voluntarily desist from rigid treatment, so that periods of cleansing through the day become less and rectal lavages are discontinued. Table 2 shows that recurrences appeared in most

of alcohol or anesthetic oils, roentgen-ray therapy and undercutting operations.

Based on this concept, a routine of management by anal hygiene and medication was instituted in 100 patients with severe pruritus ani. This simple routine of treatment directed toward preventing fecal perianal soiling resulted in subjective and objective improvement ranging from good to excellent in 93 per cent of the 80 patients who followed directions. That fecal soiling is a great factor in the causation of pruritus ani is borne out by the fact that 80 per cent of these patients reported recurrence after an interval of careless anal hygiene or after cessation of treatment.

15 East 10th Street, New York City

REFERENCES

1. Scarborough, R. A.: Pruritus ani: its etiology and treatment. *Ann. Surg.* 98:1039-1045, 1933.
2. Stone, H. B.: Pruritus ani: treatment by alcohol injection. *Surg., Gynec. & Obst.* 42:565, 1926.
3. Yeomans, F. C.; Gorsch, R. V., and Mathesheimer, J. L.: Pruritus ani with special reference to its treatment with benacol. *M. J. & Rec.* 130:279, 1929.
4. Hollander, E.: Treatment of pruritus ani by tattoo with mercuric sulfide. *Arch. Dermat. & Syph.* 38:337-339, 1938.
5. Manheim, S.: personal communication.
6. Tucker, C. C., and Hellwig, C. A.: Pruritus ani: histologic picture in forty-three cases. *Arch. Surg.* 34:929-938, 1937.
7. Caskey, C. R.: Pruritus ani. *California & West. Med.* 50:14-16, 1939.
8. Castellani, A.: Pruritus ani and pruritus vulvae of mycotic origin. *Practitioner* 117:341-355, 1926.
9. Terrell, E. H., and Shaw, F. W.: Observations on fungal infections of the peri-anal skin and rectum. *South. M. J.* 21:887-889, 1928.
10. Saul, L. J.: Incidental observations on pruritus ani. *Psychoanalyt. Quart.* 7:336, 1938.
11. Huhner, M.: Sterility and the x-rays. *J. A. M. A.* 104:1808, 1935.
12. Granet, E.: unpublished data.

REPORT ON MEDICAL PROGRESS

ABORTION

JOHN ROCK, M.D.*

BROOKLINE, MASSACHUSETTS

AN abortion is the termination of a pregnancy before extramaterial viability of the fetus is possible. Until the value to the premature baby of undisturbed comfort in a moist oxygenated, heated atmosphere and of frequent effortless feedings of small amounts of properly fortified liquids was realized, the accepted age of viability was seven months. Now that these advantages are available, it is nearer six months. Arbitrarily, then, if the conceptus dies or is extruded before the twenty-sixth week of gestation, it is considered an abortus. The word, miscarriage, really has the same meaning as abortion, and is properly used in its place, though lay usage often limits the term to abortions that are at least thought to be spontaneous in origin. Conversely it is not proper to interpret the word abortion as signifying willful interference with the pregnancy. Few medical men nowadays give the two words, abortion and miscarriage, any time significance. The extrusion of an abortus may be called either an abortion or a miscarriage, whether at the second or the twenty-sixth week of gestation.

FREQUENCY

In 1934, Kopp¹ reported that among 10,000 applicants to the birth-control clinics in New York, it was found that 29 per cent of the pregnancies

were terminated before viability, either spontaneously or by design: 1.0 abortion for every 2.5 productive confinements. Taussig² in 1931 had concluded that abortion in the United States was even more frequent than this startling estimate indicates. He computed an incidence of 31 per cent, or 1.0 abortion for every 2.3 pregnancies. In 1925, Macomber³ reported an abortion rate of only 22 per cent. Among the combined cases of Taussig and Macomber the frequency was 27 per cent. In 1938, Wiehl⁴ discovered that only 12 to 17 per cent of pregnancies were aborted. This information, however, was gathered by investigators who, uninvited, visited homes in a sample community selected for a morbidity survey. It appears that perhaps all the abortions were not frankly reported, and that the more willingly given statistics are more dependable. In 1935, Stix,⁵ from information given by almost 1000 patients in a New York birth-control clinic, found like Kopp that 30 per cent of pregnancies ended in abortion, stillbirth or ectopic disasters. The German National Bureau of Statistics⁶ reported that in 1935, 22 per cent of 300,000 hospitalized obstetric cases were abortions. How many others aborted in private is conjectural—doubtless many more than were delivered at term in homes. It is apparent that an abortion rate of 25 per cent of pregnancies is a conservative estimate.

*Research associate in obstetrics and instructor in gynecology, Harvard Medical School; visiting surgeon, Free Hospital for Women.

Induced Abortions

If 1 out of every 4 pregnancies fails, how many do so spontaneously, and how many are induced? Hamilton⁷ found that among 537 cases of abortion admitted to Bellevue Hospital, New York City, only 29 per cent were clearly spontaneous, although another 29 per cent were claimed to be, but were doubtfully so. Kopp, Stix and Taussig, and to some extent, Hamilton, justify the conclusion that about two thirds of abortions are induced. This means that about 16 per cent of pregnancies are willfully destroyed, and about 8 per cent are spontaneously aborted. Taussig⁸ quotes Plass as learning from 81 physicians in Iowa and its environs that not quite 5 per cent of pregnancies are terminated by physicians for true therapeutic reasons. From the German report already mentioned, only 0.5 per cent of 16,000 abortions were therapeutic.

Order of Pregnancies

The outrageous—or pitiable—frequency of criminal abortion makes it almost impossible to identify many of the factors of spontaneous abortion. Considering the actual causes, as I shall discuss them hereafter, it seems likely that any conceptus is but slightly, if at all, influenced by its position in a sequence of pregnancies, although the common clinical opinion is that first pregnancies are more vulnerable. To be sure, such mishaps receive undue attention.

Age of the Mother

The order of the pregnancy may not make much difference, but the age of the mother doubtless does; early miscarriage is more likely to occur in women over forty, whose endocrine balance is not as it was, and whose reproductive organs are thus not so well supported and nourished as they were before the early twilight of the menopause.

Age of Pregnancy

The transformation of a conceptus into an abortus by death or disability of all or significant parts of the organism usually precedes the attempt by the uterus to expel its useless contents by at least two, and usually by about six, weeks. When does the abortion take place? For obvious practical reasons, one must date it by the actual extrusion of most of the products of conception. Even on this basis, somewhat more than 80 per cent occur before the completion of the fourth month of gestation, most of them before the third.

ETIOLOGY

Intraovular Causes

Continuation of the careful study of aborted material started in this country, by Mall,⁹ and carried on notably by Meyer and Streeter at the Carnegie Institution, and by Hertig¹⁰ and his associates in Boston, has shown quite clearly that at least half the abortions, doubtless including even some that were induced, were made inevitable by critical deviations from normal growth of various structures at different times in the period from nidation to expulsion. There is some difference of opinion as to how frequently the observed pathologic change is due to a completely intraovular defect, by reason of abnormality in the germ plasm of either gamete, and how often it is due to interference with normal growth by maternal insufficiency of nourishment at critical stages in the development of vital tissues—perhaps of the nervous or the vascular systems. Mall⁹ leaned heavily to the latter explanation. Later studies in genetics¹¹⁻¹⁷ show quite clearly the possibility of monstrous growth from imperfect genes, a hypothesis further strengthened by the repetition of similarly defective abortuses from an individual woman.¹⁰

It may be said, then, that the primary cause of 50 per cent of spontaneous abortions is defective development of the embryo proper or of its envelopes, amnion and chorion, and that these defects are largely due to intrinsic genes of ovum or spermatozoon. The other half of abortions and, according to Mall, many of the first half already discussed, must be attributed to deficiencies in maternal nourishment and protection.

Extrinsic Maternal Causes

Properly speaking, any factor but radiant energy to affect the conceptus must first influence some organ or tissue of the mother; but because many traditional causes are primarily maternal, such as systemic diseases and endocrine dystrophies, it is customary to divide the extraovular causes of abortion into "extrinsic maternal" and "intrinsic maternal." Among the former are the following physical and chemical agents. *Radiation*, whether by x-ray or radium, in any amount greater than that needed for limited roentgenography, exposes the fetus to danger, for its nervous and vascular systems are peculiarly susceptible to the rays, indeed so much so that this means is proposed as helpfully abortifacient for therapeutic purposes.¹⁸ *Electricity* is a rare cause of abortion, but a potent one if a shocking current such as that from lightning is suffered.⁹ *Lead* passes through the placental filter into the fetal circulation and poisons

the conceptus. It more commonly causes abortion by first affecting either the ovum or more especially the spermatozoon, so that a primarily defective zygote results, that is, one that is incapable of growing to maturity.^{19, 20} *Alcohol* does little damage except so far as it disturbs the appetite and digestion and diminishes the general health of the mother and consequently the food quality of her blood.^{21, 22} *Nicotine* causes nausea before the mother can absorb enough by smoking to affect the sensitive neurovascular system of the fetus.²³

Ether or *chloroform* in excess may seriously damage the fetal respiratory or vasomotor centers respectively, but only after endangering the mother, which competent administration prevents. *Quinine*, although it possesses an oxytocic quality and is potentially deafening to the older fetus, has not been shown to precipitate abortion. On the other hand, in malaria, quinine is strongly indicated, for the plasmodia are known to accumulate in the maternal side of the placenta to the serious detriment of the fetus.²⁴

Trauma, which includes surgical procedures and coitus, is doubtless the most commonly mistaken of all the possible causes of abortion. Although often an antecedent, it can usually be excluded as a cause by careful examination of the products, which will be found to be pathologic in fully half the cases. To be actually effective, the trauma must truly institute one or more of the following factors: disturbance of the choriodecidual relation; interference with the uterine blood supply to the nidatory site; damage to membranes; serious injury to the very young corpus luteum; activation of the neuromuscular mechanism of uterine evacuation by local irritation or by cerebral disturbance. A local blow that actually injures the uterus or its major vessels or the force of which is transmitted to the placenta or an accurately directed attack on the membranes is required for traumatic abortion. By these criteria, most of the traditionally listed traumas must be considered as at most only mildly contributory to abortion. The *post hoc* resemblance of causation is made manifest by the common frequency of coitus, or of minor accidents or fright, which is such as to make it unlikely that a miscarriage—as also a fit of indigestion—could often occur without any time reference to some incidentally preceding event. This common fallacy of etiologic trauma is also discovered by examination of the abortuses, almost all of which are seen to have suffered their lethal damage many days, weeks or sometimes months before the designated injury and subsequent miscarriage occurred.

Intrinsic Maternal Causes

Infections. On the other hand, intrinsic maternal agents, those arising within the mother's body, often effect abortion. Endometritis, rarely, but systemic infection, commonly, are to blame. With influenza, pneumonia and typhoid fever, as with general septicemia and probably with brucellosis,²⁵ toxicity, anoxemia and fever²⁶⁻²⁸ are the proximal damaging factors. In malaria, as has been mentioned, the plasmodia by local accumulation figuratively smother the villi.²⁴ Tuberculosis²⁹ and syphilis³⁰ are not often causes of abortion. Appendicitis, perhaps by toxicity but more likely by peritoneal irritation, may provoke uterine contractions either before or after the operation for relief. Taussig⁸ mentions a similar neurogenous effect from urinary infection, as well as from ureteral catheterization.

Debility. Malpas,³¹ a careful British observer, asserts that "poor general health" as "manifested by anemia, debility, fatigue and loss of weight" is a common cause among habitual aborters. It is doubtless a major factor in many cases. Heart disease damages the conceptus only when it is severe enough to cause anoxemia.

Malnutrition and avitaminosis. The diet of pregnant women is apparently more important for the conservation of their own health than for that of the fetus. The studies of the blood made by Krebs and Briggs³² confirm the deductions of Nürnberger³³ in famine countries that the conceptus rarely suffers death from lack of calcium. As regards vitamins, too, one must not be misled by results obtained on laboratory animals under experimental conditions that are very rarely duplicated in human beings. Although alertly mindful of the critical importance of vitamins for the health of the mother, one must not too readily assign to a possible lack of vitamins in the diet the responsibility for abortion. In regard to vitamin E, the artificial absence of which in the diets of guinea pigs and rats causes early intrauterine³⁴⁻³⁷ death, one should defer to the authoritative Mason³⁸ who writes:

During recent years there has appeared an increasing amount of indirect evidence that a deficiency of vitamin E may be related to certain reproductive disturbances (habitual abortion, exclusive of that due to pathologic states of the uterus) both in man and in domestic animals. However, the wide distribution of vitamin E in the embryo of cereal grains, green vegetables and animal tissues, suggests that a serious deficiency of [vitamin] E is probably of relatively rare occurrence outside the experimental laboratory.

Endocrinopathy. Extensive biological investigations, together with intensive study of embryological material and abortuses, place heavy respon-

sibility on maternal endocrines for the welfare of the very young embryo, and therefore for abortion. The estrogens must condition the tube so that correct peristalsis will ensure transport of the blastocyst—not so rapidly as to deliver it to the uterus before the endometrium is properly prepared, and not so slowly as to delay its arrival on the uterine mucosa until after it needs more than the available tissue juices can give it. By either event, one may readily explain the disastrously abnormal development of the nervous or the vascular system, which is so common and which Mall believed to be due to the great susceptibility of these tissues in their earliest periods to deficiencies of nutriment. In this same category fall inadequacies of the endometrium because of improper estrogen and progesterin influence, on which the proliferation and functional activity of this mucosa depend. These two hormones not only evoke the potentiality to bleed which, when fertilization fails, is expressed by the endometrium in menstruation, but also, by a critical proportion between them, keep this bleeding mechanism under control. If, in spite of conception, excessive bleeding into the stroma around the nidatory site occurs, it must do so at first because the corpus luteum, by its progesterin, fails to inhibit the activity of the spiral arterioles, and in later stages because a defective trophoblast fails to function similarly. In even the latter event, the first cause may easily be a disturbance of maternal endocrine activity, because of which the young cytotrophoblasts were improperly nourished.

Violent emotions, however, occasionally do precipitate miscarriage. For other, more convincing reasons one may postulate that, in addition to the ovaries, the thyroid and the adrenal glands are implicated in the bleeding mechanism, and that even in the absence of a nervous disturbance, but occasionally excited by it, an intrinsic abnormality in the function of these glands may activate the local hemorrhagic diathesis.

Profound unpleasant emotions such as fear and anger have been shown to increase the secretions of the adrenal medulla so as to cause contraction of the smooth muscles of arterioles elsewhere.³⁹ Brewer^{40, 41} and others have attributed the supply of free blood to the young embryo, at least in part, to controlled alternating spasm and relaxation of the spiral arterioles of the nidatory site. It seems likely that the miscarriages that follow intense nervous shocks are actually caused by their first effect on the chromaffin tissues. Can the anterior lobe of the pituitary gland, from which come stimuli to all the other ductless glands, be involved? It is an attractive theoretical possibility, which, however, lacks adequate experimental sup-

port. Nor do the hormones, Pitressin and Pitocin from the posterior lobe of the pituitary gland apparently have any evil effect on the uterus during the first two trimesters of pregnancy, although Pitocin in the last three months may evoke effective contractions.

Uterine deformities. If malformations, malpositions, scars or tumors of the uterus are associated with disturbed vascularity of the organ, nidation may be difficult, and if accomplished it may be imperfect and lead to such abnormal growth as eventuates in early death of the conceptus. Also, although early development may be normal, such uterine derangement may so constrict the growing conceptus as to prevent its normal development and cause its premature extrusion. To irregularity in the conformation of the uterine lining, as well as to variations of nutriendency, have been attributed placental deviations, such as previa, marginata and succenturiata. The first particularly is certainly sometimes, and perhaps often, a cause of early loss of the conceptus.

Paternal Causes

As Williams⁵⁵ found in cattle, Young¹² in guinea pigs and Rugh¹⁴ in frogs, so it undoubtedly is true with human beings that defective spermatozoa may inaugurate the growth of a conceptus whose genic destiny it is to die young.

Lead is such a notorious traditional factor that pregnant women still fear the smell of paint. Geneticists⁴² suggest that minor degrees of radiation, not sufficient to stop spermatogenesis, may so distort genes as to give to the chromosomes a lethal character. Debilitated bulls frequently sire abortive fetuses.²⁵ It has not been proved that mentally or physically depleted men do likewise, but the similarity of their semen to that of faulty bulls strongly suggests that it may be true.

PROPHYLAXIS

Reference to the listed causes of abortion will suggest logical means of prophylaxis, some of which, however, are difficult or impossible to attain. It seems obvious that to prevent almost 66 per cent of abortions,—those which are induced,—economic and social and moral conditions must be improved to permit an approximate synchronization of financial security with coital irrepressibility, and that men and women must be taught first properly to evaluate reproduction, and then how harmlessly to avoid it when irremediable conditions so demand.

Against the very common intraovular defects attributable to cagogenic spermatozoa or ova, are eugenics and possibly hygiene. Proper regard to diet, exercise and rest will obviate many of the

intraovular abnormalities that are ascribed to maternal inadequacies.

Against x-rays and radium, all frequently exposed workers, men as well as women, should be protected by adequate screening. The skin of the artisan, especially, must be protected against the absorption of lead. Alcohol, tobacco, anesthetics and other drugs may be used advisedly. Surgery should be avoided when possible, and when inescapable it should be performed with deliberate regard for the sensitivity of the contractile potentiality of the fundus, for the fragility of the membranes and for the weakness of their attachments. Equanimity, even in the presence of apparent disaster, must be cultivated. Coitus should be permitted only if the cervix is safe from strong impact and the fundus is not subjected to pressure.

Curettage affords the most effective attack on the occult endometritis, which some students, notably Mall, believe to be the underlying cause of many monstrous conceptuses that are ejected. If two successive abortions have occurred, even though one or both were followed by curettage, it is advisable to curette before the inception of the next pregnancy. As prophylaxis against any systemic infection, the rules of hygiene should be rigorously followed by all, but especially by women exposed to pregnancy. To dietary inadequacies attention should also be given. A sugar-tolerance test following one abortion may give valuable help toward preventing a second. Vitamins should be given in essence if there is any gastrointestinal disorder, for such might conceivably prevent their extraction from food sources.⁴³ Milk or its constituents, in addition to vitamin D, are proverbially valuable.

The role of the endocrines in reproductive physiology makes clear their use to safeguard it. Estrogen, in daily doses equivalent to about .03 mg. given orally, will probably not interfere with ovulation as larger doses would, but will act as a tonic to tubes and uterus and may theoretically stimulate the anterior lobe of the pituitary gland to greater production of helpful gonadotropes. Estrogen, given in the last two weeks of a fertile cycle, cannot inhibit ovulation and may favorably condition the tubes and endometrium to support better the young blastocyst. During this phase, as well as periodically during the first three, four or five months of gestation, progesterone in doses about 5 mg. repeated three or four times on alternate days will at least theoretically encourage endometrial support and discourage myometrial activity. That large doses in the early weeks may interfere with the arteriolar supply of blood to the trophoblastic lacunae is a pure hypothesis. With larger doses

given after a manifest threat to abort, one must realize the danger of transforming an incomplete abortion into a missed abortion.

Small doses of thyroid held below the symptomatic level have frequently been followed by a successful pregnancy after previous sterility or abortion. To iodine, too, has been attributed success in patients with somewhat elevated basal metabolic rates. There is no dependable evidence that any available preparation of anterior pituitary hormone is of value to human beings, especially for the purpose of instituting or protecting a pregnancy. Nor can the judicious clinician say more for the chorion hormone that is extracted from pregnancy urine. Reports of its use strongly suggest that it is harmless, but do not at all prove its therapeutic value, for they cannot withstand the impartial appraisal applied by the biologist to his experiment with hormones *in vivo*. The spontaneous cure rate of abortions is high: probably 90 per cent for those diagnosed as threatened; 62 per cent in pregnancies following two previous abortions⁴¹; and probably nearer 95 per cent for those following only one abortion. A suspected aberration of the adrenal medulla may be made less likely to express itself by quiet living and the equanimity advised above, together, perhaps, with small daily doses of bromides or of one of the milder barbiturates. Sufficient avoidance of physical and mental stimuli in women who are very susceptible to functional weakness of the uterus may even require isolation and rest in bed for weeks or months.

Prophylaxis against hypoplasia is achieved by the administration of estrogen in daily doses and combined with Progestin during the last two weeks of each cycle for several months before conception. If menstruation is disturbed in rhythm or other quality by such medication, the possibility of inhibition of ovulation must be considered; if such inhibition occurs, estrogen must be diminished, especially during the first two weeks of the cycle. In the presence of sterility or following an abortion, a deformed uterus may make corrective surgery advisable.

PROCESS OF ABORTION

Since the signs and symptoms of abortion are determined by the process, insight into the behavior of abortus and uterus is indispensable to proper treatment. Certain factors affecting the process are recognized. A few of the older and larger abortuses are extruded, as are the fetus and its envelopes, at term; that is, myometrial performance precedes separation of the chorion from decidual contact. In most abortions, however, these events are transposed. Uterine cramps, before the twentieth week

at least, when unaccompanied by bleeding rarely presage miscarriage.

The condition of the products of conception has made it clear that more than half the abortions begin clinically from two to six weeks following the critical ovular catastrophe.⁴⁴ If the delay is more than eight weeks, the condition is arbitrarily termed "missed abortion." The degree and extent of the maceration that takes place during the latent period has much to do with the process of final evacuation.

Disruption of the decidua is usually the first event when ejection begins. But during the first three months, and very rarely after that, such tissue destruction may occur only in localized areas, apparently by a persistent menstrual proclivity, without separation of the normal conceptus. Such a condition is not abortion, but is appropriately called "threatened abortion." The discharge of some part of the conceptus, often only the amniotic fluid, may precede or follow the sanguineous demonstration that a large part of the decidua is disintegrated, which means that evacuation of the uterus has begun and its completion is inevitable. Frequently, this proceeds without excessive bleeding because during the delay, which is usually from two to six weeks, between death of the cyema and the beginning of extrusion, coagulation necrosis has sealed many of the decidual vessels. The abortus may appear in toto or in fragments, and there is no fixed order of progression, although with rupture of the sac usually the liquor and fetus precede. Occasionally, the passing of the whole or a part is obstructed in the cervix. During such a delay, and while ineffective contractions persist, profuse bleeding may occur, sufficient even to threaten severe shock. Because of fragmentation and possible obstruction, two details helpful in diagnosis and treatment must not be neglected: every formed particle that comes away should be most carefully recovered and inspected, a vaginal examination should be made promptly and with aseptic precautions. I see no evidence in fact, nor can I accept the theory, that proper examination is in the least likely to stimulate the processes of miscarriage, and I am equally sure that without examination much time and blood may be wasted.

DIAGNOSIS

There are truly only three kinds of abortion: incomplete (and inevitable), complete and missed. A so-called "threatened abortion" is not one until it becomes inevitable, which is not so when there is only moderate flow or rhythmic uterine cramps,

or both. A therapeutic abortion, like its criminal counterpart, is peculiar in the process of evacuation and may be at first incomplete or inevitable and later should be complete. The inevitable abortion may not always seem incomplete, for by definition this means that part of the abortus has come away, but it is so in fact, for the amount of blood that bespeaks certain inevitability appears only after extensive separation of the chorion from contact with maternal tissues. The abortion has already started, and will be completed when all contact is severed and the abortus is extruded. The transition from threatened to inevitable abortion is sometimes hard to recognize. When in doubt after examination, which should be made in any event, one should hold to the tentative diagnosis of threatened abortion. It is sometimes surprising how much blood may be lost without lethal separation of the chorion. The completeness of an abortion is certainly attested to only when the whole abortus has been recovered and identified. If these products are lost, the cessation of signs and symptoms, both of abortion and of pregnancy, is the necessary token of completeness.

The diagnosis of missed abortion is made when the outward signs of inevitable abortion have not appeared before the arbitrarily designated period of eight weeks has elapsed, after death of the cyema or cessation of growth.

TREATMENT

Abortion

The threat of abortion should be combated at the source, but unfortunately this is often obscure. Painful rhythmic contractions mean uterine irritability or excessive stimulus. Sedation with morphine or one of the barbiturates will quell the latter; progesterone in doses of 5 to 10 mg. will depress the former. Flow means disruption of the decidua by interstitial hemorrhages or separation of some of the villi from decidual contact, or both. Interdecidual bleeding during the first six weeks, and perhaps later, is doubtless due to spasm of the spiral arterioles and subsequent relaxation. This spasm may be inhibited by progesterone, again in doses of 5 to 10 mg. prudently repeated at intervals of twenty-four to forty-eight hours until two or three days after all signs have disappeared. Sedation again may be helpful by diminishing activity of the adrenal medulla, which in turn may conceivably be involved in stimulation of the arterioles. Separation of the villi may, it appears, be due to imperfect villi, the contact of which with decidua is not secure, or to excessive pressure of maternal blood in the sinuses wherein the villi lie.

The relief of pelvic congestion by confinement to bed, emptying of the lower bowel and mild sedation is rational treatment.

The attitude toward the incomplete abortion is quite the opposite. The processes of separation and evacuation should be encouraged and supplemented if necessary. Always, examination should precede treatment, for if the cervix is open and part of the abortus lies in the external os, instrumental assistance is easy and very helpful. This examination, however, should be made only after all facilities of place and equipment for handling a hemorrhage have been ensured. The hospital is the most desirable place. Posterior pituitary extract in doses of 2 to 5 mg. given intramuscularly is likely to stimulate effective contractions. Prompt surgical attack, however, is called for if bleeding is profuse, and also if the inevitable process seems to stop before completion. Hemorrhage and sepsis, as well as missed abortion, may be avoided by emptying the uterus of the defunct parasite. If the internal os is sufficiently open, the finger is safer than the curette for stripping the uterine wall; if a curette is used, it should be a large one. Posterior pituitary extract, as well as the alkaloid of ergot, should be used to prevent bleeding, which usually stops when the cavity is clean. A temporary antiseptic pack is sometimes useful if bleeding is free or prolonged.

If the complete abortus has been passed and identified as such, and if bleeding has stopped, as it usually does in such cases, curettage is not necessary. If doubt of completion arises because parts have been lost or slight bleeding persists, light curettage of the whole cavity is usually advisable.

As has been said, abortion may be precipitated by placenta previa. When this occurs before the sixteenth week, the abortus may be fragmented and removed, although the blood loss may be such as to require replacement. When, however, premonitory bleeding occurs at the twentieth week, or later, the case should be treated as one of placenta previa, and the fetus should be delivered by a Braxton-Hicks version, metreurysis or traction on the fetal scalp to tampon the placenta and accomplish slow nontraumatic dilatation of the cervix. Between the sixteenth and the twentieth week, the choice of treatment is determined by the condition of the abortus and of the degree of previa and of dilatation of the cervix.

Missed Abortion

If the latent period between death of the conceptus and evacuation of the uterus exceeds the arbitrary eight weeks, the condition is called missed abortion. Further delay disturbs the mother's endocrine balance and may lead to sepsis or hemor-

rhage, in addition to the usual malaise. Oxytocics alone are usually futile but may be very helpful in conjunction with a cervical pack or bag. If the fetus has lived for twenty weeks and the cervix is not easily dilatable, a trachelotomy is the preferred method of delivery.

Habitual Abortion

The spontaneous cure-rate among women who have had previous abortions is so high as to mislead the less perspicacious among therapists, who will be easily overwhelmed by the already flagged *post hoc* relation between treatment and events. Malpas³¹ found that 62 per cent of women who had aborted twice carried the third baby to term without specific treatment, and, similarly, 35 per cent among 25 women who had aborted three times delivered their fourth pregnancies at term. Hence, I believe, comes much of the enthusiasm for corpus-luteum hormone and for vitamin E therapy, neither of which, however, has actually been proved dangerous. Of the former, it should be said that doses of 5 mg. repeated on alternate days may inhibit the uterine contractions ordinarily evoked by death of the fetus and separation of the chorion, so that what might have been a single prompt complete miscarriage may be transformed into one of the long-drawn-out, incomplete variety, or even into a missed abortion. Possibly the greatest good that therapeutics can do for the habitual aborter is rendered during the month of conception rather than afterward. Estrogen in daily doses not exceeding .05 mg. by mouth during the whole cycle, and progesterone in bidaily injections of 5 mg. during the postovulatory phase, will theoretically condition the tubes for proper care and transport of the blastocyst, and the uterus for reception and nourishment of the trophoblast. After nidation has been accomplished, continuation of the progesterone may diminish irritability of the uterus and also any persistent menstrual urge in the spiral arterioles, thus discouraging a tendency to very early abortion. After the first month, the villi are developed and the conceptus is nourished—no longer by a secreting endometrium that depended on progesterone for stimulation, but from the maternal blood that perfuses the villous mass. Repression of the patient's corpus luteum would then suggest that the role of progesterone is over, but it has been shown that the placenta continues to produce a similar, if not an identical substance.⁴⁵ Perhaps the nonvillous chorionic membrane that lies in contact with maternal decidua depends thereon for some more direct sustenance than that derived by way of the placenta. Does the chorion supply the progesterone that keeps the maternal decidua functioning to

this end? Until we learn more of the physiology of pregnancy and of the first causes of abortion, it is reasonable to continue to use progesterone during the first half of pregnancy, or longer in some cases, if previous pregnancies have terminated in miscarriage. The great value of physical and mental hygiene should not be overlooked.

COMPLICATIONS

Hemorrhage and sepsis, as in full term deliveries, are the major complications of abortions. The former may be prevented by prompt examination under proper hospital conditions to make sure that the abortus is not caught in the cervix, and by skilful and rapid separation of what parts are attached and their prompt extraction by curette or forceps. Venoclysis of glucose solution and of blood should always be available and should be utilized freely.

Sepsis usually bespeaks illegal interference of unknown nature and extent and consequently demands the greatest caution. Again, vaginal examination should be made forthwith, for drainage may be impeded by an obstructing abortus, or possibly by a foreign body. In the absence of hemorrhage, while the temperature is 101 or only 100°F if it has been higher, or if there is pelvic inflammation, the uterus should not be entered by finger or any other instrument beyond the degree required to demonstrate an open cervical canal. Bleeding of dangerous degree, of course, takes precedence over sepsis and may demand removal of the abortus. Otherwise, medical care, including sulfathiazole in doses of 3 gm daily, while the leukocyte count exceeds 4000, plus fluids and possibly blood intravenously, is indicated. Moderate doses of oxytocics may accelerate the evacuation of the uterus. Surgery is contraindicated until the patient has recovered from sepsis; when necessary, it must be performed with consummate skill and attention to the fact that the septic uterus is perforated with the greatest of ease.

REFERENCES

- Kopp M E. *Risk Control in Practice*. 290 pp. New York: Robert M. McBride & Co., 1934. P 122.
- Tausig F J. Abortion in relation to fetal and maternal welfare. *Am J Obst & Gynec* 22:729 1931.
- Macomber D. Etiology of abortion. *Boston M & S J* 193 116-119 1925.
- Wieland D G. Summary of data on reported incidence of abortion. *Milbank Memorial Fund Quart* 16:19 1938.
- Six R K. A study of pregnancy wastage. *Milbank Memorial Fund Quart* 13:347 365 1935.
- Foreign letter from Perl n Congress of German gynecologists. *J A M A* 110:453 1938.
- Hamilton V C. Some sociologic and physiologic observations on abortion study of five hundred and thirty seven cases. *Am J Obst & Gynec* 9:919 928 1940.
- Tausig F J. *Abortion Spontaneous and Induced Medical and social aspects*. 536 pp. St. Louis: C. V. Mosby Co., 1936.
- Mall F P and Meyer A W. Studies on abortuses: a survey of pathological ova in the Carnegie Collection. *Contrib Embryol* 12:3 364 1921.
- Herrig A T. Personal communication.
- Robinson A. Discussion on the causes of early abortion and sterility. *Proc Roy Soc Med* 23:237 239 1930.
- Young W C. A study of the function of the epididymis. I. Is attainment of full spermatogenesis maturity attributable to some specific action of epididymal secretion? *J Morphol & Physiol* 47:49 495 1929. II. Importance of aging process in sperm for length of period during which fertilizing capacity is retained by sperm isolated in epididymis of guinea pig. *Ibid* 48:475 491 1929. III. Functional changes undergone by spermatozoa during their passage through epididymis and vas deferens in guinea pig. *J Exper Biol* 8:151 162 1931.
- Young W C. and Blandau R J. Ovary age and the course of gestation in the guinea pig. *Science* 84:270 1936.
- Rugh R. Effect on the embryo of a radiation of spermatozoa. *J Contraception* 4:123 125 1939.
- Williams W W. and Savage A. cited by Williams.
- Nurnberger L. cited by Goldstein L. Ovarian irradiation: a review of the experimental literature. *Am J Obst & Gynec* 16:747 762 1928.
- Little C C. and Bagg H J. The occurrence of two heritable types of abnormality among the descendants of a rayed mouse. *Am J Heredity* 10:95 989 1923.
- Mayer M D. Hartig W. and Wimpfheimer S. Therapeutic abortion by means of x ray. *Am J Obst & Gynec* 32:945 957 1936.
- Cole L J. and Bachhuber L J. The effect of lead on the germ cells of the male rabbit and fowl as indicated by their progeny. *Proc Soc Exper Biol & Med* 12:24 29 1914.
- Platt E D. Accidental complications of pregnancy from disease. In *Gynecology and Obstetrics* edited by C H Davis. Vol. I. Chap 9. 56 pp. Hagerstown, Maryland: W F Prior Co. 1938. P 37.
- MacDowell E C. The effect of light doses of alcohol upon the estrus cycle and on the number of corpora lutea and prenatal mortality in the mouse. *Proc Soc Exper Biol & Med* 21:450-485, 1924.
- MacDowell E C. Lord E M. and MacDowell C G. Heavy alcohol intoxication and prenatal mortality in mice. *Proc Soc Exper Biol & Med* 23:652 654 1926.
- Faulkner J M. Nicotine poisoning by absorption through the skin. *A M J* 100:1064 1933.
- Welsch G B. Observations on the placenta from a case of malaria. *Bull Johns Hopkins Hosp* 47:157 163 1930.
- Williams W L. Abortion in animals. *Tausig* 3:46-69.
- Nuckolls H H. and Herrig A T. Pneumococcus infection of the genital tract in women especially during pregnancy and the puerperium. *Am J Obst & Gynec* 35:782 793 1938.
- Finland M. and Dublin T D. Pneumococcus pneumoniae complicating pregnancy and the puerperium. *J A M A* 112:1027 1032 1939.
- Williams J W. *Obstetrics: A textbook for the use of students and practitioners*. Sixth edition. 1157 pp. New York: D Appleton & Co. 1931. P 58.
- Jamison E M. *Gynecological and Obstetrical Tuberculosis*. 256 pp. Philadelphia: Lea & Febiger. 1935.
- Beck A C. and Daily W T. Syphilis in pregnancy. Reprinted from Publication No 6 of the Am A Advancement Sc. Pp 101 110.
- Malpas P. A study of abortion sequences. *J Obst & Gynec Brit Emp* 49:32 949 1928.
- Krebs O S. and Briggs A P. Blood studies in normal pregnancy. *Am J Obst & Gynec* 5:67 72 1923.
- Nurnberger L. Fehlgelurt und Fruehgeburt. I. Anatomischer Teil. In *Biologie und Pathologie der Weibes* edited by J Halban and L Seitz. Vol VII part I. 982 pp. Berlin and Vienna: Urban & Schwarzenberg. 1927. P 407 562.
- Urner J A. The intra uterine changes in the pregnant albino rat (*Mus norvegicus*) deprived of vitamin E. *Anal Rec* 50:15-187, 1931.
- Idem. Section on vitamins in pregnancy. In *Obstetrics and Gynecology* edited by A H Curtis. 1165 pp. Philadelphia: W B Saunders Co., 1934. P 733 739.
- Slute E. The relation of deficiency of vitamin E to the anti proteolytic factor found in the serum of aborting women. *J Obst & Gynec Brit Emp* 43:74 86 1936.
- Idem. Observations on the aetiology of abruptio placentae and its response to vitamin E therapy. *J Obst & Gynec Brit Emp* 44:121 129 1937.
- Mason K E. Vitamins and the sex glands. In *Sex and Internal Secretions* edited by E Allen C H Danforth and E A Doisy. Second edit on 1346 pp. Baltimore: Williams & Wilkins Co. 1939. P 1184.
- Cady W B. Adrenal secretion in strong emotions and pain. In *Early Changes in Pain Hunger Fear and Rage*. Second edition. 404 pp. New York: D Appleton & Co., 1929. P 49 65.
- Brewer, J I. A normal human ovum in a stage preceding the primate streak. The Edwards Jones Brewer ovum. *Am J Anat* 61:49 481 1937.
- Brewer, J I., and Fitzgerald J E. Six normal and complete presortite human ova. *Am J Obst & Gynec* 34:210 224 1937.
- Little C C. Agents modifying germ plasma. *Surg., Gynec & Obst* 46:155 158 1928.
- Diamond L K. Personal communication.
- Streeter G L. Department of Embryology. *Carnegie Inst of Wash*. *Yearbook* 30:336 1931.
- Jones H W. and Weil P G. The corpus luteum hormone in early pregnancy report of case in which there was early removal of corpus luteum. *J A M A* 111:519 521 1938.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 26511

PRESENTATION OF CASE

A twenty-year-old student entered the hospital complaining of convulsive seizures.

The patient felt perfectly well until six days before admission, when suddenly his right hand and arm began to "tremble." The attack was of very brief duration and was not accompanied by other symptoms. The patient felt well as he went to sleep that night but some time later awoke to find his doctor bending over him and was told that he had had three convulsive seizures. These began in the right hand, spread to the arm and the entire right side of the body and finally became generalized. With the last seizure there was incontinence of urine. On awaking, the patient was nauseated, and vomited. He was admitted to another hospital that morning and in the afternoon had two similar seizures. It was noticed that at the moment the seizures became generalized the patient became unconscious. He had no more convulsive seizures during the five days before admission to this hospital, though he did have attacks of numbness of the right arm and right side of the body, together with weakness of the right arm, without loss of consciousness or convulsive movements. There had been some headaches associated with the seizures before entry, but none since. For the past year he had not done well in his schoolwork, but stated that this was due to lack of application.

The patient had had the usual childhood diseases and a tonsillectomy several years before admission. The family history was noncontributory.

On examination the patient was a fairly well-developed, thin man who answered questions promptly and sensibly. Examination of heart, lungs and abdomen was negative; the blood pressure was 118 systolic, 70 diastolic.

There was no aphasia, nor any difficulty in naming familiar objects. Visual acuity and fields were normal. There was slight, not definitely abnormal, blurring of the nasal margins of the optic disks. The right side of the face was a little less active than the left. One examiner thought that the knee jerk was more active and the abdominal reflexes less active on the left, but three days later

another examiner was unable to find any abnormal reflexes. Sensation, including stereognosis, sense of passive movement and two-point discrimination, was normal, with no difference between the two sides, and the neurological examination was negative in other respects.

The temperature, pulse and respirations were normal.

Examination of the urine was negative. Examination of the blood showed a red-cell count of 5,200,000 with a hemoglobin of 16.7 gm. (photoelectric-cell technic), and a white-cell count of 6400 with 68 per cent polymorphonuclears. A blood Hinton test was negative. A lumbar puncture gave an initial pressure of 230 mm. of spinal fluid, and a final pressure of 160 mm. after 10 cc. of clear colorless fluid had been withdrawn. This fluid contained 10 cells per cubic millimeter; 4 were polymorphonuclears and 6 were lymphocytes. It had a total protein of 32 mg. per 100 cc., with a normal gold-sol curve and a negative Wassermann test. These findings were essentially similar to those in the other hospital five days before admission.

X-ray study of the skull, mastoids and sinuses showed a definite prominence of the convolutional markings throughout the skull. The sella turcica was normal in size and shape, and the petrous and sphenoid ridges appeared normal. The pineal gland was at the posterior limits of normal in the lateral view, and in the posteroanterior view it was slightly displaced to the right. There were several areas of calcification on the left side, close to the midline, anterior to and above the pineal body.

An electroencephalographic recording revealed groups of abnormal six-cycle and four-cycle waves coming chiefly from the left frontal region.

Observation added little to the findings. The patient stated that occasionally he was unable to remember names and had difficulty in pronouncing long words, although nothing of the sort was actually observed by others and he had no difficulty in naming familiar objects or in reading or writing. The attacks of numbness in his right arm became less frequent. One attack, lasting three or four minutes, occurred while he was writing, and he found that he was unable to control movements of the right arm properly, but that he could move the arm. Headache did not recur. On the eleventh hospital day a ventriculogram showed a large mass between the cerebral hemispheres, projecting both to the right and to the left and almost obliterating the middle third of the left lateral ventricle. It was reported to have a sharply defined margin, which was slightly lobulated in its lower posterior portion. Areas of

calcification lay in the posterior portion of the mass.

An exploratory craniotomy was performed on the eleventh day.

DIFFERENTIAL DIAGNOSIS

DR. JAMES B. AYER: We are here confronted with initial symptoms of Jacksonian epilepsy, limited at first to the right hand and arm, with subsequent attacks of numbness of the whole right side of the body. The convulsive seizures were followed by loss of consciousness. The attacks of numbness were without accompanying mental impairment. Evidence for a suspected expanding lesion of the brain is at first very slight—minimal headache and slight, "not definitely abnormal" blurring of optic disks. Vomiting is not mentioned. However, when we add the evidence of the simple skull films showing prominence of the convolutional markings and the finding on lumbar puncture of a moderately elevated spinal-fluid pressure, we are entitled to consider that an expanding lesion is quite certain. If our investigation stopped at this point, we should almost surely place the lesion in or near the left frontal region, and in support of this we have the evidence offered by electroencephalography.

But we cannot place the lesion solely in the frontal area in the light of pneumography. This procedure showed a well-defined mass between the cerebral hemispheres, almost obliterating the middle portion of the left lateral ventricle, and displacing the pineal body posteriorly and to the right. Therefore we are forced to consider a mass so placed and to discuss its seat of origin, possible extension and pathologic character. I believe that certain tumors in this region may be excluded because of lack of appropriate symptomatology, that is, tumor of the pineal body, craniopharyngioma and cystic tumors of the ependyma. A mass confined to the left frontal lobe could hardly cause the x-ray picture presented.

Tumors arising in the falx, in the corpus callosum and in the septum pellucidum, including the cavum, may give this x-ray picture. Perhaps we should include an inflammatory mass because of the presence of polymorphonuclear leukocytes reported in the examination of the spinal fluid, but I prefer to regard these cells as arachnoid cells with lobulated nuclei that do resemble polymorphonuclears; a small number of such cells are commonly found in the presence of tumors involving the meninges. Tumors in the situation described cause epilepsy, but usually of a more generalized character, and we expect memory loss, apraxia and aphasia, which are not surely present.

Until of considerable size or in such a position as to block the foramen of Monro or the aqueduct, headache need not be excessive. Of the three tumors considered, I should favor a meningioma of the falx, containing calcium deposits, and I suspect that the tumor extends upward on the medial aspect of the hemispheres anteriorly, giving the focal epileptic attacks that first called attention to its presence.

DR. JAMES R. LINGLEY: The plain film shows evidence of increased pressure by prominence of the convolutional markings. The pineal body appears to be displaced backward, but on measurement it is at the posterior limits of normal. There are two small flecks of calcification above and anterior to the pineal body. These are rather difficult to see in the anteroposterior view, but stereoscopically one can make them out slightly to the left of the midline. The pineal body in this view is displaced to the right. The tumor, even on the plain films, is localized to a point close to the midline in the left midparietal region. The air studies confirm the findings of the plain film. The tumor extends down between the lateral ventricles and projects more to the left. In the anteroposterior view it appears that air in the left lateral ventricle extends around the lateral margin of the tumor, a large portion of the mass being intraventricular. It arises close to the falx, as Dr. Ayer has stated, and involves both ventricles. It could also arise in the region of the corpus callosum.

DR. AYER: I should like to ask Dr. Schwab whether the encephalograms are consistent with a tumor in that region.

DR. ROBERT S. SCHWAB: Yes.

DR. AUGUSTUS S. ROSE: Do you think that the age, twenty years, is young for meningioma?

DR. AYER: Yes, but it is also young for other forms of tumor. It is hardly a region for cholesteatoma; they usually grow from below upward, and I think Dandy's* case, arising from the fifth ventricle, showed an embryonic type of tumor. It is very rare. I accept your suggestion that the patient is young, but he is also young for glioma.

DR. JAMES C. WHITE: Epidermoid cyst, a cholesteatoma, is the guess that I should make, because of his being so young.

DR. AYER: They arise at the base, do they not?

DR. WHITE: Yes.

DR. AYER: It is a good suggestion and one that we ought to consider—some unusual form of tumor.

*Dandy, W. F.: Congenital cysts of the cavum septi pellucidum (fifth ventricle) and cavum vergae (sixth ventricle): diagnosis and treatment. *Arch. Neurol. & Psychiat.* 25:44-66, 1931.

CLINICAL DIAGNOSIS

Brain tumor.

DR. AYER'S DIAGNOSIS

Midline tumor invaginating the third and lateral ventricles by pressure from above, probably a meningioma of the falx.

ANATOMICAL DIAGNOSIS

Cholesteatoma of the third ventricle.

PATHOLOGICAL DISCUSSION

DR. CHARLES S. KUBIK: A ventriculogram was done, even though the calcium deposits were found by x-ray, because the question of intraventricular hemangioma came up. That is another tumor in which calcium may be found. Another reason for doing it was the apparent discrepancy between Jacksonian seizures beginning in the arm and calcium deposits near the midline of the parietal region. There is a considerable distance between the calcium deposits and the arm area of the motor cortex, and since a rather large tumor may have calcium in only one part of it, it was thought that the possibility of such a tumor's extending outward to the surface had to be considered.

The tumor found at operation was situated between the two hemispheres, where Dr. Ayer placed it. Dr. John S. Hodgson, who did the operation, had to go through the left lateral ventricle to reach it. The tumor was a cholesteatoma or epidermoid cyst. The contents, consisting of characteristic, flaky and cheesy material with a pearly luster, amounting in all to 20 gm., was evacuated and part of the cyst wall removed. There were two or three seizures after the operation, but no paralysis, and after the first few days convalescence was uneventful. The patient seemed to be perfectly well when he was discharged from the hospital.

Cholesteatomas usually occur at the base of the brain in the region of the sella, but may be found in other parts of the cranial cavity. The lining membrane is composed of epidermal epithelium. The other structures of the skin, such as hairs and sebaceous glands, which are seen in ordinary dermoid cysts, are not present. True dermoid cysts containing such structures, of course, may also occur within the cranial cavity. The intracapsular material in a cholesteatoma consists largely of desquamated, degenerated, squamous epithelium, has a pearly luster and, when rubbed between the fingers, feels greasy, or like soap. It contains cholesterol crystals but, unlike a dermoid cyst, no hair or sebaceous material.

DR. TRACY B. MALLORY: Have you any further comment, Dr. Ayer?

DR. AYER: Nothing, except that it is a queer place for a cholesteatoma.

DR. ALLEN G. BRAILEY: What is the prognosis?

DR. AYER: Fairly good. We have several cases that have been observed for a number of years.

CASE 26512

PRESENTATION OF CASE

First Admission. A fourteen-year-old schoolboy entered the hospital complaining of headache, nausea and vomiting following a blow on the head.

Sixteen days before admission, the patient was struck in the left occipital region with a thrown baseball and knocked down. If he lost consciousness, it was for only a few seconds. He got up and continued to play but after a few minutes complained of a headache and then began to vomit. He was taken home by his mother, who had been watching the game, and on the way she noticed that he talked vaguely and made irrelevant remarks. The boy was examined carefully by his physician, who found no abnormal physical signs, and x-ray films of the skull taken the next morning were said to be negative. However, headache and vomiting continued intermittently, the headache being especially severe in the morning. Then the headache lessened, and intermittent nausea and vomiting became the most prominent symptoms, usually recurring every other day. Between times he seemed well, was bright and ate heartily, and four days after the accident there were three successive days during which he was completely free from symptoms. Then, during the latter days before entry, drowsiness developed. Three days before admission the patient was examined by a consultant, who noted that the eyegrounds showed definite venous engorgement and a very trifling haziness at the nasal margins, which he considered to be within normal limits. Since the injury, the systolic blood pressure had averaged 118, with a diastolic between 65 and 50; the pulse rate had been between 50 and 60.

In the past the patient had had a tonsillectomy, appendectomy and mastoidectomy at unstated periods before admission. The family history was irrelevant.

On examination the patient was a well-orientated, alert, co-operative boy who did not appear ill. There was an old mastoidectomy scar behind the right ear. Examination of the heart and lungs was negative; the blood pressure was 110 systolic, 55 diastolic. Examination of the abdomen was negative except for an old appendectomy scar in

the right lower quadrant. The only positive neurological findings were a slight right facial weakness and an indeterminate right plantar reflex. The optic disks were hazier than they had been three days previously. One examiner believed that the right abdominal reflexes were less active than the left.

The temperature was 98.8°F., the pulse 56, and the respirations 20.

Examination of the urine was negative. A blood Hinton test was negative. Lumbar puncture gave an initial pressure of 230 mm. of spinal fluid; the total protein was normal (24 mg. per 100 cc.), the Wassermann test was negative, and the fluid was normal in other respects.

On the day of admission a bilateral subtemporal craniotomy was performed. The brain bulged into the wound on both sides. A considerable amount of blood-stained subdural fluid and a large amount of blood-stained subarachnoid fluid were evacuated from both sides, although there was a greater quantity of both subdural and subarachnoid fluid on the left. After removal of the fluid the brain fell back, but not so much as is usual. It was noted that the veins in the left Sylvian fissure were very large and tortuous and that one of them ran backward low down across the temporal pole. Drains were placed in both wounds, which were closed in layers with silk.

Postoperatively the patient was given 5 per cent glucose intravenously and was comfortable except for some slight vomiting. The operative wound remained clean and gradually healed while draining blood-stained fluid. The pulse remained between 50 and 70 during hospitalization, and the temperature, after an immediate postoperative rise to 100.6°F., fell to normal in three days. Five days after the operation he became less active, but not drowsy, and complained of a headache that was slightly more pronounced on the left side. Examination of the fundi showed the same blurring of the nasal margins of the optic disks that was noted preoperatively and absence of physiological cupping in the left disk. The arm jerk was thought to be a trifle more active on the right. A lumbar puncture at this time gave an initial pressure of 250 mm. of spinal fluid and a final pressure of 150 mm. after the removal of 10 cc. of clear, colorless fluid. This fluid contained no cells and had a protein content of 24 mg. per 100 cc. Another puncture three days later gave an initial pressure of 220 mm.; the fluid contained two cells and had a total protein content of 19 mg. per 100 cc. This same day, immediately after sneezing, the patient had a feeling of something giving way in his forehead in the mid-frontal re-

gion: "It clicked, and after this my head felt free and the foggy feeling disappeared." The patient was discharged on the eighteenth postoperative day, apparently relieved.

Second Admission (three weeks later). The patient had remained well until early in the morning four days before admission, when his mother saw him have a convulsion, but was unable to describe its characteristics. She summoned her physician, and within the next two hours the patient had two more convulsive seizures, each lasting one to three minutes and accompanied by loss of consciousness. The attacks began with the head turning to the right, followed by twitching of the right arm and leg and incontinence of urine. There were residual dullness, stupor, and vomiting of greenish-yellow material, and the patient complained of a frontal headache behind and above his eyes.

Neurological examination was negative except for bilateral pulsating decompression scars over the recently made burr holes, with audible systolic bruits over both. The blood pressure was 95 systolic, 60 diastolic.

The temperature and respirations were normal; the pulse was 60.

A lumbar puncture gave an initial pressure of 190 mm. of spinal fluid, with a final pressure of 170 mm. after 6 cc. of clear, colorless fluid had been removed. No cells were found in the fluid, which had a total protein of 33 mg. per 100 cc.

X-ray films of the skull were negative except for the operative defects made at the previous entry. Three electroencephalographic recordings showed an area of abnormal functioning cortex in the left frontal region extending backward to the motor area. The right side and the left side posteriorly were affected hardly at all. With mild overbreathing, the abnormality on the left side greatly increased, and finally, toward the end of overbreathing, extended to include the right side. With return to normal ventilation, the right side quickly returned to normal limits, whereas the left side remained abnormal.

An operation was performed on the ninth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. JOST MICHELSEN: The first part of this story sounds familiar. This boy received an injury to his head. Immediately following this injury there was brief unconsciousness, and after he came to, headache, vomiting and impairment of mental functions. No abnormalities were found on examination. This is the picture of a concussion or contusion of the brain, and one would expect

improvement after a few days. But the headache and vomiting continued, the headache becoming particularly severe in the morning, and drowsiness eventually developed. Both the morning headache and the drowsiness suggest that the brain lesion was not a simple concussion or contusion. Headache in the morning is characteristic of increased intracranial pressure, and the drowsiness confirms the assumption that the patient had a traumatic lesion which led to increased intracranial pressure. Why the headaches varied from day to day without apparent reason, I cannot explain, but we observe this frequently in such cases.

The findings on examination in the hospital gave some additional evidence of the increased intracranial pressure, the spinal-fluid pressure of 230 mm. being definitely abnormal. One post-traumatic lesion that would fit into the picture presented so far is an acute subdural hematoma. There are two types of posttraumatic acute subdural hematomas: one, which I should call the primary, confined to the subdural space and due to rupture of the so-called "bridging veins," and the other, the secondary, due to a contusion or laceration of the brain with subarachnoid hemorrhage that extends into the subdural space through the torn arachnoid membrane. The absence of red cells or xanthochromia in the spinal fluid is in favor of a primary subdural hematoma, but the findings at operation are not in accord with this conclusion. Blood-stained subarachnoid fluid, as well as blood-stained subdural fluid, was observed. This suggests that there was a subarachnoid hemorrhage with secondary extension into the subdural space.

The question now arises as to what this subarachnoid hemorrhage was due. Perhaps it was caused by a contusion of the brain. Since the occiput was hit, we might expect a *contrecoup* effect on the frontal lobe. The slight neurological signs—right facial weakness and right-sided reflex changes—could go with that. But there are other questions perhaps more important. Why did the brain not fall back after successful removal of the hematoma? Why was the fluid still blood-stained after sixteen days? Usually after the fifth day a spinal fluid that has contained blood clears, becomes xanthochromic and finally colorless. And how should we account for the enlargement and tortuosity of the middle cerebral veins? I shall try to answer some of these questions later on.

The recovery of the patient after the operation was not so prompt as we should expect. But this is not very unusual. Occasionally subjective and objective signs improve very slowly postoperatively.

Quite unusual, however, it seems to me, is the miracle that happened on the eighth day, when the patient sneezed and said, "It clicked, and after this my head felt free and the foggy feeling disappeared." I spent considerable time wondering about this dramatic turn of events. Sneezing increases the intracranial pressure and, even more, the pressure in the accessory sinuses of the nose. It is known to be an etiologic factor in the formation of so-called "aerocele" in posttraumatic cases.

The patient was back in the hospital three weeks later. This time the neurological examination was negative except that the pressure was still high, and that a new symptom had appeared. Four days before admission the boy had three epileptic attacks. They were of a focal character, the head turning to the right, followed by twitching of the right arm and leg and then by unconsciousness and incontinence of urine.

The electroencephalograms pointed toward the left frontal region. Clinically, the focus should have been fairly high up toward the midline anterior to the central gyrus.

Focal and generalized epileptic attacks after an injury to the brain are by no means uncommon. The period between the injury and the onset of fits is variable. There are early attacks immediately following the injury; in other cases they may develop within a month or two, or even many years later. Scar formation and atrophy of the brain are etiologic factors. But I hesitate to consider this epileptic syndrome as one of the common sequelae of a head injury. One must remember that the spinal-fluid pressure was still high. Furthermore, we are told that systolic bruits were heard over the recently made burr holes. Here we recall the enlarged veins found at operation. This leads to the conclusion that this boy had some sort of vascular abnormality, a lesion that was at least present at the time of the operation or possibly even before he received the trauma.

Vascular abnormalities of the brain vessels frequently cause epilepsy. The bruit at the time of systole might indicate that there was an arteriovenous aneurysm. Posttraumatic arteriovenous aneurysms usually involve the carotid artery and cavernous sinus after fracture of the base of the skull. They give a characteristic syndrome, which is absent here, and they do not produce epilepsy. I know of only one case of a posttraumatic arteriovenous aneurysm of the surface of the brain, which was removed by Penfield.* A venous angioma is

*Elvidge, A. R. The post traumatic convulsive and allied states. In *Injuries of the Skull, Brain and Spinal Cord* edited by Samuel Brock. 632 pp. Baltimore: Williams and Wilkins Company, 1940. P. 251.

another possibility I am unable to make a definite diagnosis

In conclusion, I should say that this boy had a traumatic lesion of the brain with subarachnoid and subdural hemorrhage followed by focal epilepsy probably associated with a vascular abnormality that was either present before the trauma or developed following it. Although very rare, an arteriovenous aneurysm in the left frontal region seems to be a reasonable bet. The somewhat common venous angioma is my second choice.

Stretching my imagination considerably further than I actually should, I might even conceive that the sneezing and the clicking had something to do with the formation of an aneurysm.

DR AUGUSTUS S ROSE: What about a subdural hematoma under the frontal lobe?

DR MICHELSEN: One thing has to be said definitely: epileptic attacks as a symptom of subdural hematoma are extremely rare. I do not know of any such cases. I have studied the literature a bit and have found that statement everywhere. I therefore eliminated from consideration a recurrence of the subdural hematoma or the possibility that some of the subdural hematoma was not drained. This might be a rare example of such a condition. However, we have not been given many details about the operation—how far down it extended, for instance. Your suggestion that further clot might be present under the frontal lobe is a very good one, because this region can not be well explored with a subtemporal opening.

DR JAMES C WHITE: We have had at least one or two such cases.

DR MICHELSEN: In the acute stage?

DR WHITE: Yes. They were relieved as soon as they were drained.

Where do you find the evidence for the subarachnoid hemorrhage? Was there blood in the spinal taps?

DR TRACY B MALLORY: At the operation, blood stained fluid was found in the subarachnoid space.

DR HENRY R VIETS: Do you know about the fields of vision?

DR CHARLES S KUBIK: They were normal.

CLINICAL DIAGNOSIS

Subdural hematoma

DR MICHELSEN'S DIAGNOSES

Contusion of the brain, with subarachnoid hemorrhage and subdural hematoma
Arteriovenous aneurysm?
Other angiomatous malformations?

ANATOMICAL DIAGNOSIS

Intradural hematoma beneath left frontal lobe

PATHOLOGICAL DISCUSSION

DR KUBIK: This is a difficult case, and it has been made more difficult by a number of "red herrings" in the clinical abstract. These, it should be added, were copied from the record in good faith and were not put in for the purpose of misleading Dr Michelsen. I should have read the copy more carefully and taken them out, since they were never thought to be important by the clinicians in charge of the patient. Considering the reported finding of a large vein at the first operation and of a bruit at the second admission, Dr Michelsen had very good reasons for his conclusions.

I agree that bloody subarachnoid fluid, observed at the first operation, is inconsistent with the finding of normal spinal fluid by lumbar puncture before operation. The small amount of blood seen in the subarachnoid space at operation must have been the result of operative trauma.

DR W JASON MIXTER ought to be here to tell you what was found at the second operation. At the first operation, burr holes were made in the usual position, and exploration did not include the anterior part of the frontal region. At the second operation, a bone flap was turned down, and an organized hematoma, from 4 to 5 cm in diameter and from 1 to 2 cm thick, was found beneath the left frontal lobe, extending nearly to the cribriform plate. This was on the outer surface of the dura and in the dura itself. The inner surface of the dura looked normal, and there was no false membrane such as is found regularly in subdural hematomas of the same age. Most of this was removed, and the boy made a good recovery.

DR MICHELSEN: Seriously, what do you think about the sneeze and the clicking in his head that is given so much space in this report?

DR KUBIK: I do not think much attention was paid to that, perhaps not so much as should have been. I do not know how to explain it. It should have been left out of the summary.

DR SAUL HERTZ: What happened to the bruit?

DR KUBIK: I think it was not heard after operation.

DR MALLORY: Dr Mixter has had a letter recently from the boy's physician stating that he is well several months postoperatively.

The New England Journal of Medicine

Formerly the
Boston Medical and Surgical Journal

Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE
ON PUBLICATIONS

Official Organ of
THE MASSACHUSETTS MEDICAL SOCIETY
THE NEW HAMPSHIRE MEDICAL SOCIETY
THE VERMONT STATE MEDICAL SOCIETY

EDITORIAL BOARD

Joseph Garland, M.D.	John P. Sutherland, M.D.
William B. Breed, M.D.	Stephen Rushmore, M.D.
George R. Minot, M.D.	Henry R. Viets, M.D.
Frank H. Lahey, M.D.	Robert M. Green, M.D.
Shields Warren, M.D.	Charles C. Lund, M.D.
George L. Tobey, Jr., M.D.	John F. Fulton, M.D.
C. Guy Lane, M.D.	A. Warren Stearns, M.D.
William A. Rogers, M.D.	Dwight O'Hara, M.D.

ASSOCIATE EDITORS

Thomas H. Lanman, M.D.	Donald Munro, M.D.
Henry Jackson, Jr., M.D.	

Walter P. Bowers, M.D., EDITOR EMERITUS
Robert N. Nye, M.D., MANAGING EDITOR
Clara D. Davies, ASSISTANT EDITOR

SUBSCRIPTION TERMS: \$6.00 per year in advance, postage paid, for the United States; Canada, \$7.04 per year; \$8.52 per year for all foreign countries belonging to the Postal Union.

MATERIAL for early publication should be received not later than noon on Saturday.

THE JOURNAL does not hold itself responsible for statements made by any contributor.

COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston, Massachusetts.

AGAIN, CHRISTMAS

As we prepare again, decorously but in a state of mind not entirely free from joyousness, to observe our most significant festival, it might be of value to glance back through the months and recall the spirit in which we passed through the days of the Advent a year ago. The particular Christmas to which we were then looking forward we believed might be the last one worth celebrating for a long time to come. The tidings were of ill omen, and the clouds that hid the future were black.

The democratic way of life was already receiving some severe body blows, not all above the belt, and the future of Christianity or of any ethical system of living looked dark indeed. An

evil spirit of unknown power was abroad, and what God had wrought seemed of little value in its path.

Then came days of panic and despair, when everything that we thought of as being right was falling, and faith crumbled. And then came the miracle of Dunkirk when a nation free in spirit arose spontaneously and went across the water and saved from destruction its beleaguered army. That was the sign that was needed, and the turning point of courage, for we knew then that where the vision fails not, the people shall not perish.

There is no question this year of where the earth's free people stand. There is no more panic or despair or fear. There is only a perfectly clear determination that on our continent at least those conditions that have fostered and idealized the spirit of Christmas shall continue to exist.

PREPAREDNESS QUESTIONNAIRES

LAST July the Committee on Medical Preparedness of the American Medical Association mailed 179,796 schedules or questionnaires to all physicians licensed in the United States and the outlying territories. On September 6, 93,437 schedules, or 52.0 per cent, had been returned, the responses varying from 83.2 per cent in Nebraska to 38.5 per cent in New Mexico. The percentage of physicians replying from the First Corps Area, which includes Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island and Vermont, was 51.3, a figure slightly lower than that for the country as a whole, whereas the percentage for those in Massachusetts was 52.8, a somewhat higher figure. Although a small number of questionnaires have undoubtedly been received during the last three months, the number of physicians who have not replied has not been materially altered.

The task of securing the balance of the desired information has been turned over to the committees on medical preparedness in the states and territories. In Massachusetts, 3732 physicians have failed to reply, and of this number approximately three fifths are members of the Massachusetts Medical Society. Schedules have been or will be forwarded to the latter by their district medi-

cal societies, and the remainder—all licensed physicians who are not members of the Society—will receive them from the headquarters of the Society

Just why there has been such a low percentage of returns is difficult to understand—approximately 90 per cent of the physicians in Canada responded to a similar request for information. Of course, the United States is not at war, however, in view of the present emergency and the attempts to prepare this country for any eventuality there seems to be little excuse for ignoring this fact finding project, voluntarily undertaken by the American Medical Association. The filling-out of the questionnaire is noncommittal, it merely furnishes accurate data that is useful at the moment and would be of extreme value in case of war. It is hoped that the response of the members of the Massachusetts Medical Society will approach 100 per cent!

MEDICAL EPONYM

FORDYCE DISEASE

John A Fordyce (1858-1925), professor of dermatology and syphilology of the Bellevue Hospital Medical College, New York City, described a peculiar affection of the mucous membrane of the lips and oral cavity in a paper by that title that appeared in the *Journal of Cutaneous and Genito-Urinary Diseases* (14: 413-419, 1896)

In the autumn of 1895 I presented to the New York Dermatological Society a physician who had consulted me for an affection of the mucous membrane of the lips and oral cavity. The patient's attention was first attracted to the condition about two years ago by a symmetrical fading of the vermilion border of the upper lip, extending from the corners of the mouth almost to the median line, leaving only a narrow margin free next to the skin and a wedge-shaped area in the center of the lip. The two patches were connected at the inferior median line, where the lips come in contact by a segment of a circle making three patches, all of uniform color, with well-defined borders and areas slightly elevated. When first noticed the color was but a shade lighter than normal, the appearance otherwise did not seem abnormal, but, by putting the tissues on the stretch, small, irregular, closely aggregated milium like bodies of a light yellow color just beneath the surface epithelium were plainly visible and completely covered the patches. I report the affection as an example of a mucous membrane change, which, while apparently not uncommon has hitherto escaped observation.

R W B

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

RAYMOND S. TITUS, M.D., *Secretary*
330 Dartmouth Street
Boston

DIABETES AND HYDRAMNIOS AS COMPLICATIONS OF PREGNANCY

Mrs. L., a thirty-eight-year-old para II with diabetes of three years' duration, was first seen in the office on March 18, 1940, when approximately six weeks pregnant.

The family history was noncontributory. The patient's past history included a tonsillectomy and an appendectomy. Diabetes was discovered in the seventh month of the first pregnancy and was controlled with insulin; the pregnancy terminated normally, the baby weighing 9 pounds, 8 ounces. In 1939 a nonmalignant cyst was removed from the left breast. Catamenia began at fourteen, were regular with a twenty-eight-day cycle and lasted four days without pain. The last period began on February 1, making the expected date of confinement November 8.

Physical examination showed a well-developed and well-nourished woman. The weight was 116 pounds. The heart was not enlarged, there were no murmurs. The lungs were clear and resonant, there were no rales. The blood pressure was 130 systolic, 70 diastolic. Vaginal examination showed the cervix posterior and the fundus anterior.

The patient was seen regularly by her obstetrician and a specialist in diabetes. The pregnancy progressed uneventfully until the twentieth week, when the blood protein level rose, the highest being 775 rat units per 100 cc. This came down under treatment with stilbesterol and Pregneninolone orally, followed by a period of stilbesterol intramuscularly and by Proluton intramuscularly.

On September 23 the patient was seen in the office. At that time the weight was 142 pounds, and the blood pressure 106 systolic, 60 diastolic. The fundus was 30 cm. above the symphysis, and the vertex was presenting. The fetal heart was audible. Vaginal examination showed the cervix to be soft, not quite flat and not open. It was thought that the patient could be induced within two or three weeks, and she entered the hospital to be under close observation.

Vaginal examination in the hospital on September 30 showed the cervix to admit a fingertip. The

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

patient's condition was perfectly satisfactory; the blood pressure was normal, and the urine showed no albumin. She had developed a hydramnios.

On October 6 uterine contractions began but subsided within a few hours. Vaginal examination on October 7 showed the cervix to be soft, practically obliterated and dilated to admit two fingers.

On October 12, when the patient was approximately thirty-seven weeks pregnant, vaginal examination showed the cervix not flat but very soft; the external os was very soft, and the internal os was dilated to admit more than two fingers; the head was high. The membranes were ruptured, with the escape of a large amount of fluid. One minim of posterior pituitary extract was injected, and labor started immediately. Two hours later the injection of another minim of pituitary extract resulted in excellent contractions, and the head came well into the pelvis. Within another two hours a simple forceps operation resulted in the delivery of a male infant weighing 8 pounds, 15 ounces. Both mother and child were in excellent condition.

The mother made an uneventful convalescence, and when seen in the office on November 23, she was very well; the weight was 121 pounds and the blood pressure 110 systolic, 60 diastolic.

Comment. This case illustrates the subsequent course of diabetes mellitus first discovered during pregnancy. That it was true diabetes was evidenced by the facts that it continued after the first delivery and that treatment with insulin was necessary.

The second pregnancy was normal except for a toxemia diagnosed by a high blood prolan. The weight increased from 116 pounds to 142 pounds three weeks before delivery. Vaginal examinations were made the last two weeks before delivery, and labor was induced three weeks before the normal estimated date of confinement, when the cervix was deemed favorable. The reasons for this early delivery were hydramnios, a large baby, the attempt to prevent intrauterine death and a knowledge that many diabetic patients do not go to full term. The mother made an uneventful convalescence, and the baby was normal in all respects.

DEATH

WILLIAMS—FREDERICK H. WILLIAMS, M.D., of Boston, died December 6. He was in his sixty-eighth year.

Dr. Williams was born in Minnesota, where he attended the University of Minnesota, later receiving his degree from the University of the South, Medical Department, Sewanee, Tennessee, in 1901. He did postgraduate work in Berlin, Germany, the New York Post-Graduate School and the London Royal Society. He was on the staffs of the Brooks, Corey Hill and Trumbull hospitals in Brook-

line. His fellowships included the Massachusetts Medical Society and the American Medical Association.

His widow, a daughter and a son survive him.

MISCELLANY

NOTES

A society of medical officers has been organized at Fort Devens under the name of the Society of the Medical Department Officers of Fort Devens for the purpose of hearing scientific papers. An election of officers was held on October 8. The following were elected: Colonel H. P. Carter, president, and Lieutenant Charles C. Verstandig, secretary-treasurer.

At the weekly meetings, papers have already been presented by Drs. E. A. Adams, Thomas H. Ham, Harry Blotner and S. J. G. Nowak. The meetings are held at the Station Hospital on Tuesday evenings at 7:30 p.m. Refreshments are served.

Medical reserve officers are invited to attend.

At the recent annual meeting of the American Academy of Dermatology and Syphilology, held at Chicago, Dr. John G. Downing, of Boston, was elected vice-president.

CORRESPONDENCE

HOMEOPATHY OVER EIGHTY YEARS AGO

To the Editor: The enclosed letter recently came into my possession and it was such interesting reading, after a lapse of eighty-two years, that I thought you might care to publish it in the *Journal*.

ROBERT D. HILDRETH, M.D.

90 Elm Street,
Westfield, Mass.

* * *

Malden, March 11th/58

Dear Br. H—,

I received yours of the 8th yesterday and was very glad to hear from old & valued friends. In regard to your medicines those marked with the cypher 0 are all too strong to use. You ought to have ordered the dilutions, instead of tinctures. Most of them should be raised to the *third* dilution before using. This is done as follows. To 1 drop of the tincture add 100 drops of Alcohol, or, taking the common half ounce vial, drop in enough of the tincture to just cover the bottom, then fill it two thirds full of pure Alcohol & shake it well. This makes the 1st dilution. Then drop from this into a clean vial as before & fill up with Alcohol for the 2nd dilution. Then drop from the 2nd into another vial & fill up as before for the 3rd.—The *Acid Sulphur* & *Nitric acid* however, must be prepared, in the 1st dilution with pure rain water, the 2nd with half water & half Alcohol, & the 3rd with pure Alcohol.—Those marked 4 are prepared with water & ought to be diluted once, making the 5th with Alcohol. Those having no mark are probably prepared for use. You can tell by the color. They should all be clear, no color but that of the Alcohol. Some of them are very dangerous in the Strong tinctures, such as Aconite, Belladonna, Conium, Nux vomica, & Helleborus.—To medicate the globules we drop enough of the proper dilution to wet them all, & shake them till all are moistened. You will need to be very careful about *labelling*, & marking the *dilution*, both on the vial & on the cork. Some might be used in acute diseases in the 1st or 2nd dilution, such as Aconite, Ipecac, Hamamelis, Sambucus & Cantha-

ns but most in the 3rd We are all pretty well, except my wife has been suffering from a severe cold or Influenza for 2 months or more My business is very good, and has been all winter The last week I charged \$44 and the week previous \$48 And during the year 1857 \$1600 But the times are hard here as elsewhere, & money hard to get We have not had much religious prosperity, or it least not many conversions the last year But we have the best of preaching, & very good meetings I feel more at home than I ever did in Westfield, I suppose because I met with so much bitter prejudice there among the members of my own church Here Homoeopathy stands as high as Allopathy, and though men have their preferences, of course, I do not meet with that bigoted, unreasonable prejudice that I did in W especially the first year or two We also enjoy many privileges & conveniences from being near the City I am glad you have at last got a Homoeopathic physician in W I hope he will be successful, & give satisfaction I should be very glad to visit Westfield again, and I ought to do so to attend to some business there, but it is next to impossible for me to get away for a single day But we are glad you think of coming this way, and we hope we shall not be disappointed of seeing you this Spring My Wife unites in love to you all, especially to Mrs H—, whom she hopes to see with you when you come She will probably go to Westfield in the course of the season if I do not If you need any further information respecting your medicines or anything else, I hope you will always feel free to write, for I shall always be happy to assist you as far as in my power Indeed I should be most ungrateful not to do so And we shall always be very happy to hear from you & yours, and much more so to see you at our house Br S— from your place staid with us night before last or Wed night Remember us to all our friends

Yours Truly
C W T—

P S The disease you have had in W which the Drs have not named, I think from your description may be easily named I should call it 'Cerebro-spinal arachnitis, or in plain English, an inflammation of the investing membrane of the brain & spinal marrow (the Arachnoid membrane) The disease probably commences about where the spinal cord enters the brain It sometimes prevails as an Epidemic The remedies are *Aconite* & *Bella donna* in frequent doses, followed if necessary by *Bryonia* and *Opium* pretty strong

C W T

SURGICAL INSTRUMENTS FOR ENGLAND

To the Editor There appeared not long ago in one of the medical publications an appeal for surgical instruments for the American surgeons who are working in England The request made me sit up and take notice. What medical man has not some old instruments that are not being used, since others have taken their place? Why cannot medical men follow the good example of Uncle Sam? He is supplying battleships to kill Hitlerism Why cannot we do the same? Not all of us can do surgery, not all of us can leave our families and enlist in the cause of humanity However, every one of us can find some thing in our offices that may be of great use to the medical and surgical men and women who are risking their lives by working under all the hazards of shell and fire to save humanity

The writer is happy to state that he recently delivered to The British War Relief Society at 203 Clarendon Street, Boston, such items as a floor lamp, an irrigator, basins, a

desk lamp and various instruments, as well as some ampules of medications

Let every reader right now—today, not tomorrow—go over carefully all the instruments which are not used in the office I am sure that thousands of instruments will be found that would be of great use to our colleagues on the other side of the Atlantic, who are jeopardizing their lives for us By all means let us do our share by showing them that we are with them At the same time let us do our bit in helping to make this world a safe and sane place for the human race

WILLIAM FRANKMAN, M D

736 Hancock Street,
Wollaston, Massachusetts

REPORTS OF MEETINGS

TRUDEAU SOCIETY OF BOSTON

A meeting of the Trudeau Society of Boston was held on October 24, 1940, at the Beth Israel Hospital Dr Alton Pope presided The meeting was addressed by Dr Richard H Overholt, who talked on the subject, 'The Treatment of Lung Abscess

In reviewing the literature, the speaker found that the mortality rate for this disease under medical treatment varied from 34 to 75 per cent, the cure rate from 7 to 50 per cent Combined medical and surgical management showed a 35 per cent mortality and only 50 per cent cures Surgical management alone was likewise disappointing To rule out the possibility that the reported hospital cases were poor risks, the results from 100 private cases were gathered from competent clinicians In this series, there were 31 deaths, and only 49 patients became asymptomatic

In a recent publication, Dr Harold Neuhof and his associates reported 104 consecutive cases in which external drainage was provided early in the course of the disease In this group, there were 4 deaths The sound pathological and surgical principles on which this excellent work is founded and the superior results obtained led to an adoption of the same course by Dr Overholt Since so doing, the mortality in early cases has dropped to 7 per cent, and the cure rate has risen to 93 per cent thus patients with residual symptoms were eliminated

The series of 95 cases reported by Dr Overholt included all types of pulmonary suppuration with cavitation, such as pulmonary gangrene and apurid and putrid pulmonary abscesses Excluded were those of a tuberculous nature, those secondary to a pulmonary tumor, or those primarily a part of a generalized pyemia or secondary to an unquestioned bronchiectasis

Study of the bacteriology of lung abscesses revealed most frequently a mixture of aerobic and anaerobic organisms The importance of adequate oxygenation in dealing with anaerobes is obvious, and the speaker pointed out the rationale of opening such cavities to the air and the use of oxygen forming zinc peroxide to change the putrid abscess wall to a healthy granulating surface

At operation, in practically all cases a mass of semisolid, caseous debris was found filling the abscess cavity The speaker pointed out the improbability of complete healing of such a process by other than surgical drainage

Of the 95 cases studied, 91 were found to border on one of the pleural surfaces Pleural symphysis was found in all but one The upper posterior portion of the lower lobe was the most frequent location accounting for almost two thirds of the total Although a definite cavity could not always be demonstrated roentgenographically, its presence was always confirmed at operation

Instead of dividing cases into acute and chronic on a chronological basis, Dr. Overholt preferred to classify them into simple and complicated. Simple abscesses included either single or multilocular processes, usually of short duration but without daughter abscesses, surrounding bronchiectasis or marked pulmonary fibrosis. Conversely, complicated cases included those with daughter abscesses, marked bronchiectasis or pulmonary fibrosis.

The safety of surgical drainage is based on two factors, accurate localization and avoidance of traversing the surrounding zone of pneumonitis or neighboring healthy pulmonary tissue. Accurate roentgenological localization is accomplished by obtaining films taken in varying positions. When the surface projection is localized, a few minims of a mixture of carbon and Lipiodol is injected into the overlying intercostal muscle. The Lipiodol can be visualized by roentgenography for confirmation, and the carbon can be seen at operation, thus providing a definite landmark. By such accurate localization, the abscess can be drained without traversing the "danger zone" of surrounding pneumonitis or normal lung parenchyma. In cases in which the danger zone was accidentally invaded, the mortality rate rose from 7 to 27 per cent.

A one-stage drainage is the treatment of choice. Only for those abscesses facing the interlobar fissure or other pleural surface not in contact with the chest wall is a two-stage procedure necessary. The technic consists in making a small incision over the abscess and resection of a short segment of one rib. The subcutaneous fascia and intercostal structures are sewn together to seal off the fascial planes and thus prevent a dissecting infection of the chest wall. Should no pleural adhesions be found, extrapleural dissection is carried out to determine the location, and drainage is through this site. After the presence of pleural symphysis has been determined, positive-pressure oxygen is administered by the anesthetist, and a small opening is made into the abscess. The detritus is removed. The cavity and wound are packed with gauze soaked in zinc peroxide, and the patient is placed on the operated side on the litter. Only then is the positive pressure released. It is believed that the positive pressure tends to keep the lung in apposition with the chest wall and thus prevents tearing the pleural adhesions. It also forces the contents of the cavity toward the outside and prevents spillover infection to the same or contralateral lung.

Since this technic was adopted, the incidence of empyema has been 4 per cent in 43 cases, in contrast to 16 per cent in the former two-stage plan of treatment. Furthermore, there has been no case of cellulitis of the thoracic wall.

In conclusion, Dr. Overholt emphasized the importance of early drainage. Once the diagnosis is established and localization accomplished, nothing will be gained by delay. Procrastination leads to complicated cases with a drop in the cure rate and a rise in the mortality rate. Reports in the literature indicated that of the fatal cases 73 per cent were classed as "frankly hopeless" within the first month. It was also found that in a group of 205 reported cases, the average duration of the disease preoperatively was four hundred and six days. Natural remissions that occur during the course of the disease should not lull the physician into a sense of security, but in the light of recent statistics should lead him to early surgical drainage while an uncomplicated condition exists that can be treated by a method with a low mortality and a high cure rate.

The discussion was opened by Dr. Theodore L. Badger, of the Boston City Hospital, who pointed out that the 30 per cent of lung abscesses that cure themselves spontaneously are the basis for "expectant" medical treatment, which has now become active. In the last two years the cure rate has improved from 3 to 55 per cent by increasing the postural drainage and using chemotherapy in the form of nearsphenamine, bismuth and sometimes sulfanilamide. By using postural drainage every two hours during the day and every four hours at night there have now been complete cures in 5 consecutive patients. Chemotherapy was the result of a bacteriological study that showed fusospirochetal invasion in all autopsied cases at the Boston City Hospital. These invade much farther than any roentgen evidence demonstrates, and thus may contraindicate surgery. Dr. Badger stated that not all surgeons are competent, and since one can tell in two or three weeks what the medical outcome will be, one is justified in inaugurating this therapy at least temporarily. He stressed the importance of oral hygiene in general, particularly preoperatively, as a preventive measure.

Dr. Henry L. Cabitt, of the Beth Israel Hospital, suggested that lung abscess was a surgical problem like any other abscess. He deplored the fact that only 10 of 72 cases had been treated surgically within six weeks of onset, whereas Dr. Neuhof had operated on 86 of 100, and Dr. Overholt on 50 per cent. He also pointed out that there was a great discrepancy in size between the abscesses that he saw and those described by these workers.

Dr. Donald S. King, of the Massachusetts General Hospital, asked when operation should be carried out on the basis of Graham's description of the formation of a lung abscess, which states that the cavity does not appear for two to six weeks, when a pyogenic membrane is formed. He therefore suggested surgery in five to six weeks if the patient is not improving rapidly on a medical regimen. The large early mortality mentioned by so many observers is often accompanied by widespread pneumonitis when surgery would be of no avail, he claimed.

Dr. John W. Strieder, of the Boston City Hospital, stated that the finding of all types of pathologic processes simultaneously in lung abscess precludes the possibility of classifying this disease according to Dr. Overholt and of treating them all by one method. Of 28 cases in the last two years, he had operated on only 1 in less than eight weeks after onset. A two-stage procedure was invariably employed, and a cavity always easily found at the second stage. The mortality was 14 per cent, but many patients have residual disease.

The meeting was concluded by Dr. Overholt, who emphasized that bacterial infection was insignificant if early operation was employed, and that the only cases given preoperative treatment were those already in the complicated stage. In regard to time of operation, the speaker stated that these cases were considered to be emergencies and that the patients were operated on just as soon as the cavity was demonstrated. Cavities have been seen as early as ten days after tonsillectomy, in refutation of the Graham theory. The duration of hospitalization has averaged twenty-six days, in contrast to the former period of eighty-seven days. Dr. Overholt stated that the area of cavitation is not necessarily in the center of the area of pneumonitis, and that postural drainage may be employed to allow air to enter an otherwise blocked cavity and thus aid in localization. Otherwise postural drainage has been contraindicated.

Instead of dividing cases into acute and chronic on a chronological basis, Dr. Overholt preferred to classify them into simple and complicated. Simple abscesses included either single or multilocular processes, usually of short duration but without daughter abscesses, surrounding bronchiectasis or marked pulmonary fibrosis. Conversely, complicated cases included those with daughter abscesses, marked bronchiectasis or pulmonary fibrosis.

The safety of surgical drainage is based on two factors, accurate localization and avoidance of traversing the surrounding zone of pneumonitis or neighboring healthy pulmonary tissue. Accurate roentgenological localization is accomplished by obtaining films taken in varying positions. When the surface projection is localized, a few minims of a mixture of carbon and Lipiodol is injected into the overlying intercostal muscle. The Lipiodol can be visualized by roentgenography for confirmation, and the carbon can be seen at operation, thus providing a definite landmark. By such accurate localization, the abscess can be drained without traversing the "danger zone" of surrounding pneumonitis or normal lung parenchyma. In cases in which the danger zone was accidentally invaded, the mortality rate rose from 7 to 27 per cent.

A one-stage drainage is the treatment of choice. Only for those abscesses facing the interlobar fissure or other pleural surface not in contact with the chest wall is a two-stage procedure necessary. The technic consists in making a small incision over the abscess and resection of a short segment of one rib. The subcutaneous fascia and intercostal structures are sewn together to seal off the fascial planes and thus prevent a dissecting infection of the chest wall. Should no pleural adhesions be found, extrapleural dissection is carried out to determine the location, and drainage is through this site. After the presence of pleural symphysis has been determined, positive-pressure oxygen is administered by the anesthetist, and a small opening is made into the abscess. The detritus is removed. The cavity and wound are packed with gauze soaked in zinc peroxide, and the patient is placed on the operated side on the litter. Only then is the positive pressure released. It is believed that the positive pressure tends to keep the lung in apposition with the chest wall and thus prevents tearing the pleural adhesions. It also forces the contents of the cavity toward the outside and prevents spillover infection to the same or contralateral lung.

Since this technic was adopted, the incidence of empyema has been 4 per cent in 43 cases, in contrast to 16 per cent in the former two-stage plan of treatment. Furthermore, there has been no case of cellulitis of the thoracic wall.

In conclusion, Dr. Overholt emphasized the importance of early drainage. Once the diagnosis is established and localization accomplished, nothing will be gained by delay. Procrastination leads to complicated cases with a drop in the cure rate and a rise in the mortality rate. Reports in the literature indicated that of the fatal cases 73 per cent were classed as "frankly hopeless" within the first month. It was also found that in a group of 205 reported cases, the average duration of the disease preoperatively was four hundred and six days. Natural remissions that occur during the course of the disease should not lull the physician into a sense of security, but in the light of recent statistics should lead him to early surgical drainage while an uncomplicated condition exists that can be treated by a method with a low mortality and a high cure rate.

The discussion was opened by Dr. Theodore L. Badger, of the Boston City Hospital, who pointed out that the 30 per cent of lung abscesses that cure themselves spontaneously are the basis for "expectant" medical treatment, which has now become active. In the last two years the cure rate has improved from 3 to 55 per cent by increasing the postural drainage and using chemotherapy in the form of nearsphenamine, bismuth and sometimes sulfanilamide. By using postural drainage every two hours during the day and every four hours at night there have now been complete cures in 5 consecutive patients. Chemotherapy was the result of a bacteriological study that showed fusospirochetal invasion in all autopsied cases at the Boston City Hospital. These invade much farther than any roentgen evidence demonstrates, and thus may contraindicate surgery. Dr. Badger stated that not all surgeons are competent, and since one can tell in two or three weeks what the medical outcome will be, one is justified in inaugurating this therapy at least temporarily. He stressed the importance of oral hygiene in general, particularly preoperatively, as a preventive measure.

Dr. Henry L. Cabitt, of the Beth Israel Hospital, suggested that lung abscess was a surgical problem like any other abscess. He deplored the fact that only 10 of 72 cases had been treated surgically within six weeks of onset, whereas Dr. Neuhoof had operated on 86 of 100, and Dr. Overholt on 50 per cent. He also pointed out that there was a great discrepancy in size between the abscesses that he saw and those described by these workers.

Dr. Donald S. King, of the Massachusetts General Hospital, asked when operation should be carried out on the basis of Graham's description of the formation of a lung abscess, which states that the cavity does not appear for two to six weeks, when a pyogenic membrane is formed. He therefore suggested surgery in five to six weeks if the patient is not improving rapidly on a medical regimen. The large early mortality mentioned by so many observers is often accompanied by widespread pneumonitis when surgery would be of no avail, he claimed.

Dr. John W. Strieder, of the Boston City Hospital, stated that the finding of all types of pathologic processes simultaneously in lung abscess precludes the possibility of classifying this disease according to Dr. Overholt and of treating them all by one method. Of 28 cases in the last two years, he had operated on only 1 in less than eight weeks after onset. A two-stage procedure was invariably employed, and a cavity always easily found at the second stage. The mortality was 14 per cent, but many patients have residual disease.

The meeting was concluded by Dr. Overholt, who emphasized that bacterial infection was insignificant if early operation was employed, and that the only cases given preoperative treatment were those already in the complicated stage. In regard to time of operation, the speaker stated that these cases were considered to be emergencies and that the patients were operated on just as soon as the cavity was demonstrated. Cavities have been seen as early as ten days after tonsillectomy, in refutation of the Graham theory. The duration of hospitalization has averaged twenty-six days, in contrast to the former period of eighty-seven days. Dr. Overholt stated that the area of cavitation is not necessarily in the center of the area of pneumonitis, and that postural drainage may be employed to allow air to enter an otherwise blocked cavity and thus aid in localization. Otherwise postural drainage has been contraindicated.

FRANKLIN

JANUARY 14.

MARCH 11.

MAY 13.

Meetings will be held at 11 a.m. at the Franklin County Hospital, Greenfield.

NORFOLK

JANUARY 28 — Carney Hospital.

FEBRUARY 25 — Medicolegal meeting. 8:30 p.m. Hotel Puritan, Boston.

MARCH 25 — To be announced.

MAY 8 — Censors' meeting. Hotel Puritan.

SUFFOLK

JANUARY 29 — Page 604, issue of October 10.

APRIL 30 — Page 604, issue of October 10.

WORCESTER

JANUARY 8 — Worcester City Hospital, Worcester.

FEBRUARY 12 — Worcester State Hospital, Worcester.

MARCH 12 — Memorial Hospital, Worcester.

APRIL 9 — Hahnemann Hospital, Worcester.

Supper at 6:30 p.m. followed by a business meeting and scientific program.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

The Successful Error: A critical study of Freudian psychoanalysis. By Rudolf Allers, M.D., Ph.D., professor of psychology, School of Philosophy, Catholic University of America, and former reader in psychiatry in the medical schools of the Universities of Munich and Vienna. 8°, cloth, 266 pp. New York: Sheed & Ward, Inc., 1940. \$3.00.

Medical Genetics and Eugenics. By Charles B. Davenport, B.S., A.B., A.M., Ph.D.; Clyde E. Keeler, B.S., M.A., M.S., Sc.D., fellow of the Wistar Institute, Philadelphia; Maude Slye, A.B., Sc.D. (Hon.), director of the Cancer Laboratory, Otho S. A. Sprague Memorial Foundation, University of Chicago; and Madge Thurlow Macklin, A.B., M.D., LL.D., associate professor of anatomy, Western Ontario Medical School, London, Ontario, Canada. 8°, cloth, 141 pp., with 59 illustrations. Philadelphia: Woman's Medical College of Pennsylvania. \$1.00.

Fractures and Dislocations for Practitioners. By Edwin O. Geckeler, M.D., fellow of the American Academy of Orthopaedic Surgeons and diplomate of the American Board of Orthopaedic Surgery. Second edition. 8°, cloth, 314 pp., with 267 illustrations. Baltimore: Williams & Wilkins Company, 1940. \$4.00.

Taber's Cyclopedic Medical Dictionary: Including a digest of medical subjects. By Clarence Wilbur Taber. 12°, cloth, 1372 pp., with 273 illustrations. Philadelphia: F. A. Davis Company, 1940. \$2.50.

Studies from the Rockefeller Institute for Medical Research. Vol. 116. 4°, cloth, 609 pp., with 135 tables, 77 figures, 69 plates and 13 charts. New York: Rockefeller Institute for Medical Research, 1940. \$2.00.

Loose-Leaf Specialties in Medical Practice. Vol. II. *Dermatology and Syphilis.* 8°, paper, 172 pp. New York: Thomas Nelson & Sons, 1940.

The Neuroses in War. By several authors under the editorship of Emanuel Miller, M.A. (Cantab.), M.R.C.P., D.P.M. (Cams.), with a concluding chapter by H. Crichton-Miller, M.D., F.R.C.P. 8°, cloth, 250 pp. New York: Macmillan Company, 1940. \$2.50.

Practical Handbook of the Pathology of the Skin: An introduction to the histology, pathology, bacteriology and mycology of the skin, with special reference to technique. By J. M. H. Macleod, M.A., M.D., F.R.C.P. (Lond.), physician and honorary director, Pathological Department, St. John's Hospital for Diseases of the Skin, physician for skin diseases, Hospital for Tropical Diseases, and consulting physician for diseases of the skin, Charing Cross Hospital; and I. Muende, M.B., B.S., B.Sc. (Lond.), pathologist in charge of Out-Patients' Clinic and lecturer in pathology, St. John's Hospital for Diseases of the Skin, and dermatologist, Middlesex County Council, Willesden General Hospital, Evelina Hospital for Sick Children and Princess Elizabeth of York Hospital for Children. Second edition. 8°, cloth, 415 pp., with 27 colored and 125 black-and-white illustrations. New York: Paul B. Hoeber, Incorporated, 1940. \$9.00.

Organization, Strategy and Tactics of the Army Medical Services in War. By Lieut.-Colonel T. B. Nicholls, M.B., Ch.B., Royal Army Medical Corps (retired), medical officer, A.R.P., Derbyshire County, late deputy assistant director of hygiene and pathology, Northern Ireland District, assistant director of hygiene, Southern Command, India, and assistant director of hygiene and pathology, Eastern Command. With chapters by Air-Commodore A. S. Glynn, M.B., Ch.B., K.H.S., R.A.F., P.M.O., fighter command, R.A.F.; Colonel A. R. Laurie, M.B., Ch.B., D.M.R.E. (T.A.), A.D.M.S., second antiaircraft division; and Colonel F. G. Lescher, M.C., M.A., M.D., M.R.C.P. (T.A.), group officer, E.M.S. Second edition. 8°, cloth, 488 pp. London: Baillière, Tindall and Cox, 1940. Obtainable in the United States from Williams and Wilkins Company. \$5.00.

Landmarks and Surface Markings of the Human Body. By L. Bathe Rawling, M.B., B.Sch. (Cantab.), F.R.C.S., consulting surgeon to St. Bartholomew's Hospital. Eighth edition. 8°, cloth, 98 pp., with 36 illustrations. New York: Paul B. Hoeber, Incorporated, 1940. \$3.00.

Controlled Fertility: An evaluation of clinic service. By Regine K. Stix, M.D., research associate, Milbank Memorial Fund; and Frank W. Notestein, Ph.D., lecturer, School of Public Affairs, Princeton University. 8°, cloth, 201 pp., with 56 tables and 16 illustrations. Baltimore: Williams and Wilkins Company, 1940. \$3.00.

BOOK REVIEWS

Menstrual Disorders: Pathology, diagnosis and treatment. C. Frederic Fluhmann, M.D., C.M. 8°, cloth, 329 pp., with 119 illustrations. Philadelphia: W. B. Saunders Company, 1939. \$5.00.

This book is an attempt to systematize the physiology and pathology of menstruation and its disorders in the light of the newer endocrine knowledge. One wonders whether this can be successfully done while our knowledge of the endocrine glands and their interrelations is still so imperfect; this is not intended as a criticism of the book, since it is well written and well documented and represents a valuable reference book, but one that must later be supplemented or replaced. The material dealing with the concepts of menstruation, the menarche, the menstrual

story of experimental embryology is inextricably interwoven with the general history of embryology, and for that reason it is incorrect to say that "until 1859 embryologists were content to follow changes in form" or to assert categorically that "Roux was the creator of experimental embryology."

The excellent bibliography is worthy of careful study. There are approximately 385 references, of which about 140 belong to the twentieth century, 135 to the nineteenth century, 65 to the eighteenth century and 45 to the seventeenth century.

Despite minor errors, apparently now familiar to the author, the reader will easily recognize that Dr. Meyer combines with his ability to present the material in a critical, provocative manner a deep sympathetic knowledge of his subject. Considered from the point of view of another contribution to the history of science, this volume gives added weight to the following words of Professor George Sarton*: "The latest results are like the new fruits of a tree; the fruits serve our immediate practical purposes, but for all that, it is the tree that matters."

Students, teachers and all libraries should own a copy of this valuable book.

*Sarton, G.: *The History of Science and the New Humanism*. 216 pp. Cambridge, Massachusetts: Harvard University Press, 1937. P. 5.

A Textbook of Pathology. By W. G. MacCallum, M.D. Seventh edition, thoroughly revised. 8°, 1302 pp., with 697 illustrations. Philadelphia: W. B. Saunders Company, 1940. \$10.00.

This is the seventh edition of what may be called the most scholarly textbook of pathology in the English language. Published first in 1916, this book broke with tradition in the organization of its contents. There is no division into general and special pathology. The reaction of various parts or systems of the body to injuries, such as obstruction, bacterial diseases, disturbances of fat metabolism or local disturbances in the circulation of the blood, forms the basis of this method of teaching. Throughout the book, stress is placed on the causes of disease and their effects in disturbing the functions of the body. The illustrations are all of high caliber, and they do much to clarify the subject matter. The style throughout is clear and readable.

Professor MacCallum has revised his book in the light of developments since the last edition four years ago. Consideration is given to the world literature in the treatment of the subject matter. The experiences and critical judgment of the author, however, are evident on every page. Nowhere in the text does the author fail to live up to the statement of Goethe that he chose for his preface: "It is only when we know very little about a subject that we are quite sure; and with knowledge, doubt arises and grows." For the thoughtful student a better introduction to the study of disease could not be chosen.

The Emperor's Itch: The legend concerning Napoleon's affliction with scabies. By Friedman 8°, cloth, 82 pp., with 10 pl. York: 1940. \$1.50.

For over one hundred many that the skin irri-
parte suff. scabi-
a derm. ho in
ease, h. im-
the co: the
hern-
Nap

been c
N
w
ively
and
scabi
th

Toulon and suffered from it for the succeeding nine or ten years. At the end of this period, he engaged the well-known French physician, Corvisart, as his private doctor. It is reported that under Corvisart's direction the symptoms rapidly abated, although it seems certain that Napoleon was never permanently free of pruritic crises. Such crises occurred while he was at St. Helena and caused him to seek relief by excoriating his skin. Incidentally, Dr. Friedman believes that the characteristic pose assumed by Napoleon, with his right hand under his waistcoat, was not the result of his skin eruption, but a mannerism cultivated from his earliest days. Finally, it is pointed out that the medicine used by Corvisart has no effect on scabies or on dermatitis herpetiformis. Napoleon's confidence in his physician enabled Corvisart to apply psychotherapeutic measures, a method often useful in treating dermatitis.

This book is an interesting study, carefully worked out by an expert in the field. There are numerous illustrations, not all of them particularly well reproduced. The text is written in a straightforward style, occasionally with an amusing touch. The author tends to overemphasize his own conclusions, and thus the book must be considered as a personal record rather than a carefully considered historical document.

The general appearance of the book needs comment: the format is not pleasing, and much of the printing is poor. Furthermore, the author has allowed the publisher undue liberties which do not bring credit to either.

Diathermie Chirurgicale. By Dr. C.-A. Arraud. 8°, paper, 216 pp., with 52 illustrations. Paris: Gauthier-Villars, 1939. 50 Fr. fr.

The first seven pages of this book are a brief but inclusive résumé of the history of the subject from d'Arsonval to Howard Kelly. An orderly discussion of high-frequency currents and the various types of electrodes, both monopolar and bipolar, then follows. The section on long-wave and short-wave currents is particularly good. A brief rather optimistic chapter compares electric coagulation with freezing, electrolysis and x-ray and radium therapy. Finally the products of various French manufacturers are reviewed.

The author discusses the use of physiotherapy in cancer. The discussion is good so far as small external cancers are concerned; beyond that the material is unsound, at least from the point of view of American medicine. The chapter on various affections of the skin is overenthusiastic, particularly in the treatment of pigmented moles and keloids. The reviewer believes that it is extremely dangerous to treat pigmented moles in the fashion the author recommends. To treat varicose veins by diathermy, as is strongly advised, seems ridiculous.

The treatment of carcinoma in gynecological conditions is sound, but to recommend electric coagulation as an adjunct is open to question. The section on transurethral resection of the prostate is particularly good; however, the reviewer cannot share the author's enthusiasm in the treatment of cancer of the rectum.

The discussion of the use of diathermy in the nose and throat is adequate except that the author recommends the destruction of tonsils. This is contrary to what is considered the best surgical procedure in America. His treatment of the subject of diathermy in ophthalmology is also to considerable question.

The book is badly bound and printed, but written in an original manner. The author is obviously an enthusiast, and his recommendation of various forms of treatment.

story of experimental embryology is inextricably interwoven with the general history of embryology, and for that reason it is incorrect to say that "until 1859 embryologists were content to follow changes in form" or to assert categorically that "Roux was the creator of experimental embryology."

The excellent bibliography is worthy of careful study. There are approximately 385 references, of which about 140 belong to the twentieth century, 135 to the nineteenth century, 65 to the eighteenth century and 45 to the seventeenth century.

Despite minor errors, apparently now familiar to the author, the reader will easily recognize that Dr. Meyer combines with his ability to present the material in a critical, provocative manner a deep sympathetic knowledge of his subject. Considered from the point of view of another contribution to the history of science, this volume gives added weight to the following words of Professor George Sarton*: "The latest results are like the new fruits of a tree; the fruits serve our immediate practical purposes, but for all that, it is the tree that matters."

Students, teachers and all libraries should own a copy of this valuable book.

*Sarton, G.: *The History of Science and the New Humanism*. 216 pp. Cambridge, Massachusetts: Harvard University Press, 1937. P. 5.

A Textbook of Pathology. By W. G. MacCallum, M.D. Seventh edition, thoroughly revised. 8°, 1302 pp., with 697 illustrations. Philadelphia: W. B. Saunders Company, 1940. \$10.00.

This is the seventh edition of what may be called the most scholarly textbook of pathology in the English language. Published first in 1916, this book broke with tradition in the organization of its contents. There is no division into general and special pathology. The reaction of various parts or systems of the body to injuries, such as obstruction, bacterial diseases, disturbances of fat metabolism or local disturbances in the circulation of the blood, forms the basis of this method of teaching. Throughout the book, stress is placed on the causes of disease and their effects in disturbing the functions of the body. The illustrations are all of high caliber, and they do much to clarify the subject matter. The style throughout is clear and readable.

Professor MacCallum has revised his book in the light of developments since the last edition four years ago. Consideration is given to the world literature in the treatment of the subject matter. The experiences and critical judgment of the author, however, are evident on every page. Nowhere in the text does the author fail to live up to the statement of Goethe that he chose for his preface: "It is only when we know very little about a subject that we are quite sure; and with knowledge, doubt arises and grows." For the thoughtful student a better introduction to the study of disease could not be chosen.

The Emperor's Itch: The legend concerning Napoleon's affliction with scabies. By Reuben Friedman, M.D. 8°, cloth, 82 pp., with 10 plates. New York: Froben Press, 1940. \$1.50.

For over one hundred years it has been considered by many that the skin irritation from which Napoleon Bonaparte suffered was scabies. Dr. Friedman, well known as a dermatologist, who has written extensively on this disease, has now investigated this problem and has come to the conclusion that the disease was probably dermatitis herpetiformis.

Napoleon is supposed to have developed the disease at

Toulon and suffered from it for the succeeding nine or ten years. At the end of this period, he engaged the well-known French physician, Corvisart, as his private doctor. It is reported that under Corvisart's direction the symptoms rapidly abated, although it seems certain that Napoleon was never permanently free of pruritic crises. Such crises occurred while he was at St. Helena and caused him to seek relief by excoriating his skin. Incidentally, Dr. Friedman believes that the characteristic pose assumed by Napoleon, with his right hand under his waistcoat, was not the result of his skin eruption, but a mannerism cultivated from his earliest days. Finally, it is pointed out that the medicine used by Corvisart has no effect on scabies or on dermatitis herpetiformis. Napoleon's confidence in his physician enabled Corvisart to apply psychotherapeutic measures, a method often useful in treating dermatitis.

This book is an interesting study, carefully worked out by an expert in the field. There are numerous illustrations, not all of them particularly well reproduced. The text is written in a straightforward style, occasionally with an amusing touch. The author tends to overemphasize his own conclusions, and thus the book must be considered as a personal record rather than a carefully considered historical document.

The general appearance of the book needs comment: the format is not pleasing, and much of the printing is poor. Furthermore, the author has allowed the publisher undue liberties which do not bring credit to either.

Diathermie Chirurgicale. By Dr. C.-A. Arraud. 8°, paper, 216 pp., with 52 illustrations. Paris: Gauthier-Villars, 1939. 50 Fr. fr.

The first seven pages of this book are a brief but inclusive résumé of the history of the subject from d'Arsonval to Howard Kelly. An orderly discussion of high-frequency currents and the various types of electrodes, both monopolar and bipolar, then follows. The section on long-wave and short-wave currents is particularly good. A brief rather optimistic chapter compares electric coagulation with freezing, electrolysis and x-ray and radium therapy. Finally the products of various French manufacturers are reviewed.

The author discusses the use of physiotherapy in cancer. The discussion is good so far as small external cancers are concerned; beyond that the material is unsound, at least from the point of view of American medicine. The chapter on various affections of the skin is overenthusiastic, particularly in the treatment of pigmented moles and keloids. The reviewer believes that it is extremely dangerous to treat pigmented moles in the fashion the author recommends. To treat varicose veins by diathermy, as is strongly advised, seems ridiculous.

The treatment of carcinoma in gynecological conditions is sound, but to recommend electric coagulation as an adjunct is open to question. The section on transurethral resection of the prostate is particularly good; however, the reviewer cannot share the author's enthusiasm in the treatment of cancer of the rectum.

The discussion of the use of diathermy in the nose and throat is adequate except that the author recommends the destruction of tonsils. This is contrary to what is considered the best surgical procedure in America. His treatment of the subject of diathermy in ophthalmology is also open to considerable question.

The book is badly bound and printed, but written in an orderly fashion. The author is obviously an enthusiast, and goes too far in his recommendation of various forms of physical treatment.

diameters of the inlet as criteria, there was no greater variation than 0.5 cm. between the two technics. The accuracy of the Thoms method has been proved at operation by Thoms himself and also by Schuman,⁵ who in 1936 reported 50 cases measured at laparotomy; the Thoms technic was accurate within 2 mm. or less.

The study included in this report concerned the routine measuring of 200 unselected primiparas and a correlation of the findings.

The x-ray measurements of the fetal heads were compared with the actual dimensions obtained at the time of birth and proved to be of definite practical value. By assuming a gain in mean circumference of 0.32 cm. and in occipitofrontal diameter of 0.25 cm. weekly during the last month,—according to the law of uniform fetal growth ratios as established by Scammon and Calkins,⁶—one can anticipate fairly accurately the size of the fetal head at the time of labor, even when the films have been taken three or four weeks before delivery. In cases where the head was engaged when the films were taken, the measurements, as a rule, varied less than 0.5 cm. from the actual dimensions. If the head was floating there was an occasional discrepancy up to 1.0 cm. in the mean circumference or 0.5 cm. in the occipitofrontal diameter, but in the large majority of cases the head measurements were sufficiently accurate for making a practical appraisal of the size of the presenting part. In cases of breech presentations the head measurements were of no value.

The contour of the inlet, which is delineated so clearly by the Thoms technic, is not shown so well by the simple anteroposterior film with the patient flat on the table; the inlet is at an angle rather than directly parallel to the film. However, since enough of the fore-pelvis can be seen to gain a general idea of the type-tendency, one can diagnose the type quite correctly by supplementing the anteroposterior, lateral, anterior and posterior sagittal diameters of the inlet. A folded sheet under the lumbar region when the anteroposterior film is taken helps considerably in demonstrating the contour of the inlet. In borderline cases one may add to the anteroposterior and lateral films a third view, that with the patient semirecumbent in the manner of the Thoms technic, in order to visualize more accurately the inlet configuration.

TECHNIC

The technic of measurement is as follows:

Take anteroposterior and lateral films, using a standard target-film distance (we use the 75-cm. or 30-in. distance described by Ball). Place films (14 by 17 in.) transversely

for both views. In the anteroposterior position, a folded sheet is placed under the small of the back, and in the lateral position under the side of the chest, to minimize the distortion of the image of the contour of the inlet. In the lateral position, the thighs are extended so that the femurs do not overshadow the symphysis. Shadows of the ischial tuberosities are included on this film. Sketch in the ischial spines and ischial tuberosities, and then mark points between each of these pairs of bony landmarks. Sketch in the inner border of symphysis.

The various diameters and corrections are as follows:

Anteroposterior Diameter of Inlet. From the promontory of the sacrum to the superoposterior limit of the symphysis.

Transverse Diameter of Inlet. The widest transverse measurement of the inlet on the anteroposterior film.

Anterior Sagittal Diameter of Inlet. From the posterosuperior surface of the symphysis to the point of bisection of the anteroposterior diameter by the transverse diameter.

Posterior Sagittal Diameter of Inlet. From the point of bisection of the anteroposterior diameter by the transverse diameter to the promontory of sacrum.

Anterior Sagittal Diameter of Mid-Pelvis. From the posteroinferior border of the symphysis to the interspinous point.

Posterior Sagittal Diameter of Mid-Pelvis. The continuation of the anterior sagittal line from the interspinous point to where it meets either the sacrum or coccyx.

Bispinous Diameter of Mid-Pelvis. A line drawn between the medial margins of the shadows of the ischial spines on the anteroposterior film.

Pubotuberous Diameter. A line drawn at right angles from the anteroposterior diameter of the inlet to the intertuberous point.

Correction Factor for Pelvic Measurements in Mid-Sagittal Plane. (Anteroposterior diameter of inlet, anterior and posterior sagittal diameters of inlet and mid-pelvis, and pubotuberous diameter.) The distance from the symphysis to 1.2 cm. lateral to the medial limit of the greater trochanter of the femur.

Correction Factor for Transverse Diameter of Inlet. The distance from the spinous process of the first sacral segment to a point on the anteroposterior diameter of the inlet where it is bisected by a line parallel to the height of the sacrum and drawn from the interspinous point.

Correction Factor for Bispinous Diameter. The distance from the interspinous point to a point 1.2 cm. posterior to the sacrum or coccyx on the same plane with the interspinous point.

Correction Factor for Circumference of Head in Lateral Film. The distance from the center of the calvarium in the anteroposterior view to meet a line drawn from the wing of the ilium to the described point on the greater trochanter of the femur.

Correction Factor for Occipitofrontal Diameter of Head and Circumference of Head in Anteroposterior Film. The distance from the center of the calvarium in the lateral film to the spinous process of the first sacral segment.

To the various correction factors derived from the films one then adds the tabletop-film distance. The special calculator, the slide rule or the formula is then brought into play for the necessary mathematics required in reducing the magnified

diameters of the inlet as criteria, there was no greater variation than 0.5 cm. between the two technics. The accuracy of the Thoms method has been proved at operation by Thoms himself and also by Schuman,⁵ who in 1936 reported 50 cases measured at laparotomy; the Thoms technic was accurate within 2 mm. or less.

The study included in this report concerned the routine measuring of 200 unselected primiparas and a correlation of the findings.

The x-ray measurements of the fetal heads were compared with the actual dimensions obtained at the time of birth and proved to be of definite practical value. By assuming a gain in mean circumference of 0.32 cm. and in occipitofrontal diameter of 0.25 cm. weekly during the last month, — according to the law of uniform fetal growth ratios as established by Scammon and Calkins,⁶ — one can anticipate fairly accurately the size of the fetal head at the time of labor, even when the films have been taken three or four weeks before delivery. In cases where the head was engaged when the films were taken, the measurements, as a rule, varied less than 0.5 cm. from the actual dimensions. If the head was floating there was an occasional discrepancy up to 1.0 cm. in the mean circumference or 0.5 cm. in the occipitofrontal diameter, but in the large majority of cases the head measurements were sufficiently accurate for making a practical appraisal of the size of the presenting part. In cases of breech presentations the head measurements were of no value.

The contour of the inlet, which is delineated so clearly by the Thoms technic, is not shown so well by the simple anteroposterior film with the patient flat on the table; the inlet is at an angle rather than directly parallel to the film. However, since enough of the fore-pelvis can be seen to gain a general idea of the type-tendency, one can diagnose the type quite correctly by supplementing the anteroposterior, lateral, anterior and posterior sagittal diameters of the inlet. A folded sheet under the lumbar region when the anteroposterior film is taken helps considerably in demonstrating the contour of the inlet. In borderline cases one may add to the anteroposterior and lateral films a third view, that with the patient semirecumbent in the manner of the Thoms technic, in order to visualize more accurately the inlet configuration.

TECHNIC

The technic of measurement is as follows:

Take anteroposterior and lateral films, using a standard target-film distance (we use the 75-cm. or 30-in. distance described by Ball). Place films (14 by 17 in.) transversely

for both views. In the anteroposterior position, a folded sheet is placed under the small of the back, and in the lateral position under the side of the chest, to minimize the distortion of the image of the contour of the inlet. In the lateral position, the thighs are extended so that the femurs do not overshadow the symphysis. Shadows of the ischial tuberosities are included on this film. Sketch in the ischial spines and ischial tuberosities, and then mark points between each of these pairs of bony landmarks. Sketch in the inner border of symphysis.

The various diameters and corrections are as follows:

Anteroposterior Diameter of Inlet. From the promontory of the sacrum to the superoposterior limit of the symphysis.

Transverse Diameter of Inlet. The widest transverse measurement of the inlet on the anteroposterior film.

Anterior Sagittal Diameter of Inlet. From the posterosuperior surface of the symphysis to the point of bisection of the anteroposterior diameter by the transverse diameter.

Posterior Sagittal Diameter of Inlet. From the point of bisection of the anteroposterior diameter by the transverse diameter to the promontory of sacrum.

Anterior Sagittal Diameter of Mid-Pelvis. From the posteroinferior border of the symphysis to the interspinous point.

Posterior Sagittal Diameter of Mid-Pelvis. The continuation of the anterior sagittal line from the interspinous point to where it meets either the sacrum or coccyx.

Bispinous Diameter of Mid-Pelvis. A line drawn between the medial margins of the shadows of the ischial spines on the anteroposterior film.

Pubotuberous Diameter. A line drawn at right angles from the anteroposterior diameter of the inlet to the intertuberous point.

Correction Factor for Pelvic Measurements in Mid-Sagittal Plane. (Anteroposterior diameter of inlet, anterior and posterior sagittal diameters of inlet and mid-pelvis, and pubotuberous diameter.) The distance from the symphysis to 1.2 cm. lateral to the medial limit of the greater trochanter of the femur.

Correction Factor for Transverse Diameter of Inlet. The distance from the spinous process of the first sacral segment to a point on the anteroposterior diameter of the inlet where it is bisected by a line parallel to the height of the sacrum and drawn from the interspinous point.

Correction Factor for Bispinous Diameter. The distance from the interspinous point to a point 1.2 cm. posterior to the sacrum or coccyx on the same plane with the interspinous point.

Correction Factor for Circumference of Head in Lateral Film. The distance from the center of the calvarium in the anteroposterior view to meet a line drawn from the wing of the ilium to the described point on the greater trochanter of the femur.

Correction Factor for Occipitofrontal Diameter of Head and Circumference of Head in Anteroposterior Film. The distance from the center of the calvarium in the lateral film to the spinous process of the first sacral segment.

To the various correction factors derived from the films one then adds the tabletop-film distance. The special calculator, the slide rule or the formula is then brought into play for the necessary mathematics required in reducing the magnified

and round types were very frequent. Many mixed types were found, particularly pelvis with an android tendency in either the fore-pelvis or the

TABLE 1. *Types of Pelves.*

TYPE OR TENDENCY	INCIDENCE
	%
Gynecoid	65.0
Round	20.0
Android	7.0
Flat	4.5
Anthropoid	3.0
Asymmetrical	0.5

posterior pelvis. The classification of our series is shown in Table 1.

The incidence of the various types of pelvis, according to our statistics, differs from those of

we believe are more important from an anthropological than an obstetric viewpoint.

External measurements, which were done routinely on all cases, proved of but slight value in diagnosing the type of pelvis or in ascertaining the correct anteroposterior diameter of the inlet. However, external palpation and mensuration of the subpubic arch and outlet were of unquestionable value. In only 20 per cent of our cases was

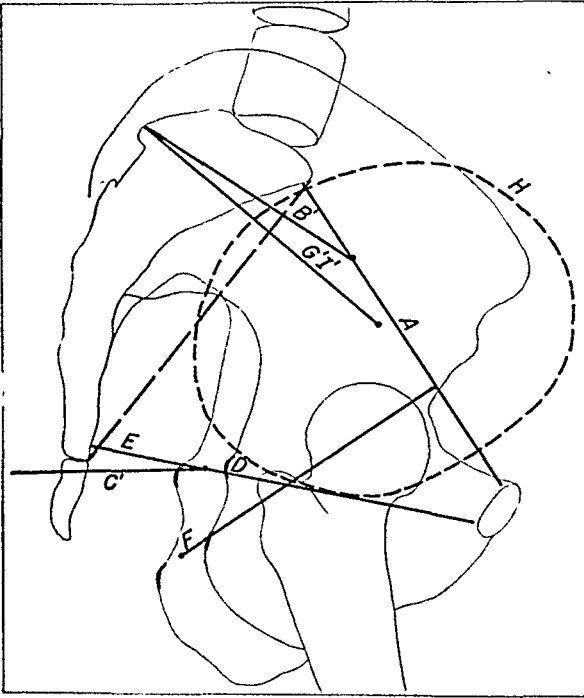


FIGURE 2.

A = anteroposterior diameter of the inlet; D = anterior sagittal diameter of the mid-pelvis; E = posterior sagittal diameter of the mid-pelvis; F = pubotuberous diameter or length of fore-pelvis; H = circumference of the head in lateral view; B' = from the point of bisection of the anteroposterior and transverse diameters of the inlet (this point is obtained by a line drawn parallel to that representing the height of the sacrum and from the interspinous point) to the spinous process of first sacral segment; G' = from the center of the calvarium to the spinous process of first sacral segment; C' = from the interspinous point to a point $\frac{1}{2}$ inch posterior to the sacrum or coccyx on the same plane with the interspinous point.

Thoms and of Caldwell and Moloy mainly because with their method of visualization they were able to note the less obvious differences in contour that



FIGURE 3.

A male type of fore-pelvis preventing the engagement of the head; the anteroposterior and transverse measurements of the inlet were normal.

the conjugate vera, as determined from the measurement of the external conjugate, within 0.5 cm. of the measurement by x-ray, and in some cases there was a discrepancy of 4.0 cm. or more. In no case was the conjugate vera, as measured by x-ray, smaller than the measurement computed from the external conjugate. As a corollary to this latter finding we can assume that if the external conjugate is ample, which usually means 18.5 cm. or over, the conjugate vera must be adequate; on the other hand, an external conjugate under 18.5 cm. does not necessarily indicate an inadequate conjugate vera. However, one must be mindful that in the android pelvis the length of the conjugate vera is no criterion of the capacity of the inlet to allow engagement of the head, because of the angulation of the fore-pelvis.

The work of Jacobs,⁹ with use of his inclinometer to measure the anteroposterior diameter of the inlet, has detracted considerably from the value of the diagonal conjugate in determining the diameter of the conjugate vera. On several of our films we have checked the influence of the inclination of the symphysis on the length of the diagonal conjugate, and have found Jacobs's conclusions to be quite accurate.

and round types were very frequent. Many mixed types were found, particularly pelvis with an android tendency in either the fore-pelvis or the

TABLE 1. *Types of Pelvès.*

TYPE OR TENDENCY	INCIDENCE %
Gynecoid	65.0
Round	20.0
Android	7.0
Flat	4.5
Anthropoid	3.0
Asymmetrical	0.5

posterior pelvis. The classification of our series is shown in Table 1.

The incidence of the various types of pelvis, according to our statistics, differs from those of

we believe are more important from an anthropological than an obstetric viewpoint.

External measurements, which were done routinely on all cases, proved of but slight value in diagnosing the type of pelvis or in ascertaining the correct anteroposterior diameter of the inlet. However, external palpation and mensuration of the subpubic arch and outlet were of unquestionable value. In only 20 per cent of our cases was

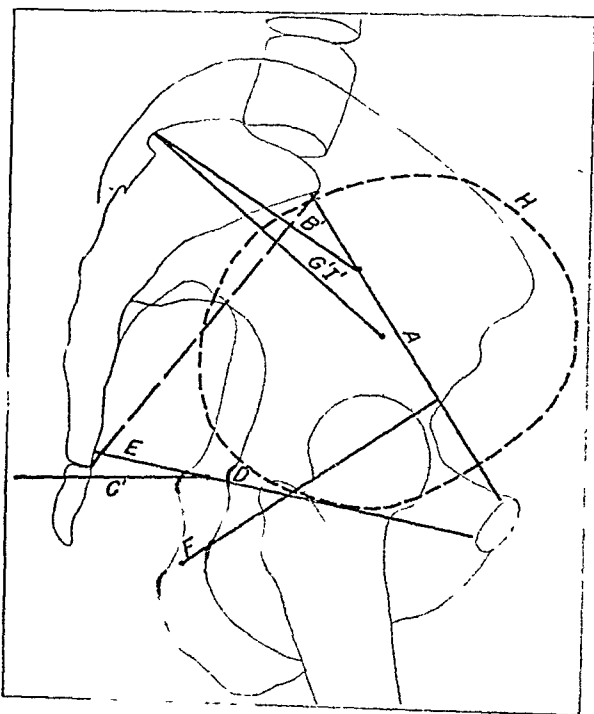


FIGURE 2.

A = anteroposterior diameter of the inlet; D = anterior sagittal diameter of the mid-pelvis; E = posterior sagittal diameter of the mid-pelvis; F = pubotuberous diameter or length of fore-pelvis; H = circumference of the head in lateral view; B' = from the point of bisection of the anteroposterior and transverse diameters of the inlet (this point is obtained by a line drawn parallel to that representing the height of the sacrum and from the interspinous point) to the spinous process of first sacral segment; G' = from the center of the calvarium to the spinous process of first sacral segment; C' = from the interspinous point to a point $\frac{1}{2}$ inch posterior to the sacrum or coccyx on the same plane with the interspinous point.

Thoms and of Caldwell and Moloy mainly because with their method of visualization they were able to note the less obvious differences in contour that

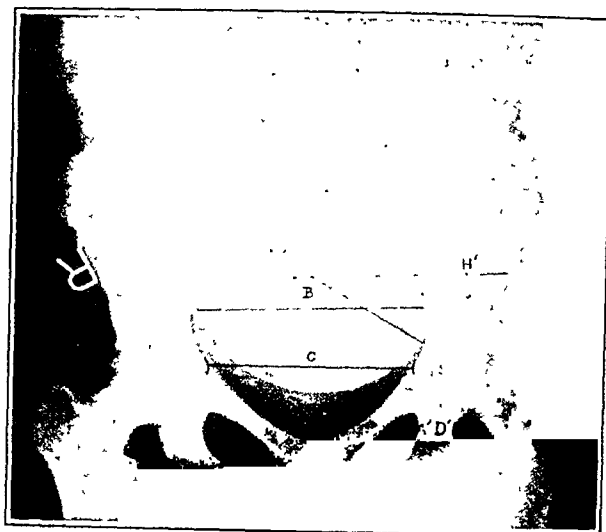


FIGURE 3.

A male type of fore-pelvis preventing the engagement of the head; the anteroposterior and transverse measurements of the inlet were normal.

the conjugate vera, as determined from the measurement of the external conjugate, within 0.5 cm. of the measurement by x-ray, and in some cases there was a discrepancy of 4.0 cm. or more. In no case was the conjugate vera, as measured by x-ray, smaller than the measurement computed from the external conjugate. As a corollary to this latter finding we can assume that if the external conjugate is ample, which usually means 18.5 cm. or over, the conjugate vera must be adequate; on the other hand, an external conjugate under 18.5 cm. does not necessarily indicate an inadequate conjugate vera. However, one must be mindful that in the android pelvis the length of the conjugate vera is no criterion of the capacity of the inlet to allow engagement of the head, because of the angulation of the fore-pelvis.

The work of Jacobs,⁹ with use of his inclinometer to measure the anteroposterior diameter of the inlet, has detracted considerably from the value of the diagonal conjugate in determining the diameter of the conjugate vera. On several of our films we have checked the influence of the inclination of the symphysis on the length of the diagonal conjugate, and have found Jacobs's conclusions to be quite accurate.

The problem of prognosticating the ability of a certain fetal head to engage in a given pelvic inlet involves more than a consideration of the diameters concerned and cannot be reduced to a mathematical formula. Due consideration must be given to the contour of the inlet, the angulation of the fore-pelvis, the flattening of the posterior pelvis, the encroachment of the promontory on the transverse diameter, the resistance offered by the cervix and its influence in directing the head into the larger or smaller part of the pelvis, the degree of flexion and the moldability of the head, the strength of the uterine contractions and other factors.

In this series we encountered 2 cases, elderly primiparas with adequate pelves, who required cesarean section because of fetal distress after several hours' test of labor, with failure of the cervix to dilate and nonengagement of the fetal head.

Transverse Diameter of Inlet

The transverse diameters of the inlet varied from 10.5 to 14.5 cm., the majority being over 12 cm., as shown in Table 4. The fact that no

TABLE 4. Length of Transverse Diameters.

LENGTH	INCIDENCE
	%
13 cm. and over	25
12-13 cm.	49
11-12 cm.	25
Under 11 cm.	1

transverse diameter was under 10.5 cm. suggests that, in our series at any rate, this diameter could not be a cause of dystocia.

Where there is a male type of posterior pelvis, with the greatest transverse diameter of the inlet approximating the promontory by less than 3 cm., one must measure the available transverse diameter at least 3 cm. from the promontory; otherwise, one may get a false concept of the roominess of the inlet

Caldwell, Moloy and D'Esopo¹¹ have shown that in all types of pelves except the anthropoid 70 per cent of the cases have the head entering the inlet in the occipitotransverse position. Therefore, if a head is well flexed as it presents at the inlet, the suboccipitobregmatic diameter of 9.5 cm. is offered for engagement with a generally adequate transverse diameter of the inlet. This fact renders the biparietal diameter of 9.0 to 9.5 cm. the important fetal diameter to be considered in most cases in relation to the conjugate vera.

Bispinous Diameter or Transverse Diameter of Mid-Pelvis

The bispinous diameter between the tips of the ischial spines, which constitutes the transverse and

also the narrowest diameter of the mid-pelvis, varied in our series from 7.6 to 12.5 cm., the majority being 10 cm. or over, as shown in Table 5.

Assuming a diameter of 9.5 cm. to be adequate even for posterior heads, 81 per cent of the cases were in this category. The narrower diameters were found to be causes of dystocia, not per se,

TABLE 5. Length of Bispinous Diameter.

LENGTH	INCIDENCE
	%
10 0 cm. or over	56 0
9 5-10 0 cm.	25 0
9 0-9 5 cm.	10 5
8 5-9 0 cm.	7 5
Under 8 5 cm.	1 0

but only in association with a narrow postero-sagittal diameter of the mid-pelvis and a narrow subpubic arch. The narrow bispinous diameters were found usually in the pelves with an android tendency in the posterior portion of the inlet, and in the funnel-shaped pelves. When the occiput is anterior, the bitemporal diameter of 8.0 cm. presents in this diameter, and consequently in anterior positions the bispinous diameter is invariably adequate. In occiput posterior positions the biparietal diameter presents in the bispinous diameter. If the latter is 9.0 cm. or under, there is a tendency toward an unrotated posterior occiput or mid-transverse arrest, provided there is also a narrow subpubic arch, so that the head, when it reaches the mid-pelvis, may not find room under a wide arch to allow it to recede from the narrow bispinous diameter.

Posterior Sagittal Diameter of Mid-Pelvis

The posterior sagittal diameter of the mid-pelvis, which constitutes the width of the greater sciatic notch on a level with the ischial spines, varied from 2.4 to 6.2 cm. Eighty-six per cent of the cases were 3.5 cm. or over, which seems to be normal (Table 6).

The posterior sagittal diameter of the mid-pelvis is important to allow the rotation of posterior occipital presentations. If the occiput is posterior and there is a narrow subpubic arch combined with a bispinous diameter of 9 cm. or less, at least 3 cm. is needed in the posterior sagittal diameter to permit rotation. This type of complication is usually seen in the male types of pelves. For all practical purposes, the posterior sagittal diameter, to be adequate for rotation, should measure at least one third of the bispinous diameter.

In considering the mid-pelvis, one must also be aware of the sacrococcygeal platform and its angulation and relation to the planes of the ischial spines. If the coccyx is markedly angulated at its junction

with the sacrum, or if the concavity of the lower sacrum and coccyx encroaches too much on the plane of the mid pelvis, a quasi platform may

TABLE 6 Length of Posterior Sagittal Diameter of Mid-Pelvis

LENGTH	INCIDENCE %
4 cm or over	65
3.5-4.0 cm	21
3.0-3.5 cm	13
Under 3 cm	1

be formed to hinder descent of the head, and dilatation of the cervix, with consequent arrest at the mid-pelvis, endangering the fetal cerebrum

Pubotuberous Diameter

The pubotuberous diameter, suggested by Schuman,¹¹ which is really the perpendicular length of the fore pelvis, varied from 65 to 108 cm. (Table 7). The large majority of cases (73 per

TABLE 7. Length of Pubotuberous Diameter.

LENGTH	INCIDENCE %
10.5 cm or over	1
9.5-10.5 cm	26
9.0-9.5 cm	38
Under 9 cm	35

cent) measured 9.5 cm. or less, leaving 27 per cent as potentially funnel in type. The minority usually accompanied the pelvis with an android or anthropoid tendency. The pubotuberous measurement is particularly important in cases where a narrow subpubic arch, associated with a long pubotuberous diameter, may present an apparently adequate bituberous or transverse diameter of the outlet. In such cases, measurement of the bituberous diameter alone provides an incorrect conception of the adequacy of the pelvis, owing to the masking of the narrow subpubic arch by the abnormally long pubotuberous diameter. In many cases a wide subpubic arch, with a short pubotuberous diameter, compensates for a narrow bituberous diameter and affords an easy egress for the head.

CONCLUSIONS

The use of x-ray films in pelvimetry has added a more scientific aspect to obstetrics and enables one to prognosticate more confidently the role that the pelvis will play in each obstetric problem. We believe that in the vast majority of cases a test of labor should be given, but the time of the test will vary markedly with the character of the maternal pelvis involved. To perform a cesarean sec-

tion on the basis of the data obtained from measurements alone, unless the conjugate vera is 7 cm or less, is to minimize the astounding faculty of Nature to effect delivery from below, even in the presence of apparently insurmountable obstacles. To anticipate an easy labor because of ample measurements is to discount the influence of the cervix, the uterine contractions and the general constitution of the patient in the conduct of labor. Neither the duration of labor nor the probability of operative delivery can be anticipated by consideration of the pelvis alone, because of the variability of the other factors involved. X-ray measurements are but a part of the general picture and to the experienced accoucheur are of distinct value in following the course of labor and helping to indicate when and how to use instrumental intervention.

X-ray pelvimetry should not supplant external and internal measurements and palpation, but should supplement them in questionable cases. Every primipara does not require x-ray pelvimetry, but in the following cases we believe that the procedure is indicated: primiparas with floating heads at term; multiparas with a history of previous difficult deliveries; primiparous breeches, with apparently small pelves by external measurements; cases with narrow subpubic arches and outlets, in order to determine the adequacy of the mid pelvis; elderly primiparas with external conjugates of 18.5 cm or less, so that one can more readily differentiate bony from soft tissue dystocia when the patient is in labor.

47 Bay State Road

REFERENCES

- 1 Ball R P Pelviccephalography *Am J Obst & Gynec* 32 249 1937
- 2 Idem Pelviccephalometry *Radiology* 31 188 1937, 1938
- 3 Snow W and Lewis F A simple technique and new instrument for rapid roentgen pelvimetry *Am J Roentgenol* 43 132 1930
- 4 Thomas H *The Obstetric Pelvis* 115 pp Baltimore Williams & Wilkins Co 1935 Oometrical significance of pelvic variations study of four hundred and fifty primiparous women *Brit M J* 2 210 212 1937
- 5 Thomas H and Wilson H M Roentgen methods for routine obstetrical pelvimetry *Yale J Biol & Med* 10 437 444 1938
- 6 Schuman E A Size and shape of pelvis in relation to direct measurement *Am J Obst & Gynec* 32 832 835 1936
- 7 Scammon R E and Calkins L A *Development and Growth of the External Dimensions of the Human Body in Fetal Period* 367 pp Minneapolis University of Minnesota Press 1929
- 8 Caldwell W E and Moloy H C Anatomical variations in the female pelvis and their effect in labor with a suggested classification *Am J Obst & Gynec* 26 419 505 1933
- 9 Caldwell W E, Moloy H C and D'Esopo D A Further studies on the pelvic architecture *Am J Obst & Gynec* 28 482 497 1934
- 10 Jacobs J B Borderline pelvis *Am J Obst & Gynec* 33 775 787 1937
- 11 Irving F C *A Textbook of Obstetrics for Students and Practitioners* 558 pp New York The Macmillan Co 1936
- 12 Caldwell W E, Moloy H C and D'Esopo D A Roentgenologic study of the mechanism of engagement of the fetal head *Am J Obst & Gynec* 28 824 841 1934 Further studies on the mechanism of labor *Idem* 30 763 814 1935 Studies on the pelvic arrests *Idem* 36 928 961 1938 The role of the lower uterine soft parts in labor *Idem* 32 727 753 1936
- 13 Schuman E A New measurement (clinical) for estimating depth of the true pelvis. Preliminary communication *Am J Obst & Gynec* 28 497 500 1934

PRACTICAL PSYCHIATRY WITH ADOLESCENTS

II. Technic of Psychiatric Investigation for the General Practitioner

DANIEL J. SULLIVAN, M.D.,* AND OTTO BILLIG, M.D.†

ASHEVILLE, NORTH CAROLINA

A RECENT article¹ called the attention of the general practitioner to the problems of adolescence; it emphasized the need for mental hygiene methods in handling these cases. The general survey of the field was outlined, including illustrative case histories, and general recommendations were made as to the part the general practitioner could and should play in helping this type of patient. A surprising number of requests were received for further information and reference material, and several of these inquiries described difficulties that physicians have had with their own children. In view of the apparent need for further elaboration, it has been decided to describe in this paper a technic of psychiatric investigation for the needs of the general practitioner, and in a subsequent paper to describe the technic of psychotherapy, with appropriate case histories, and to suggest a program of reading on the subject of the adolescent and his problems.

GENERAL CONSIDERATIONS

Psychiatric investigation in the adolescent may be entered into at once if the patient comes, or, as more often happens, is brought by the parents, to the physician because of some disturbance of mood or conduct in the home. In general, one should obtain the history first, do a routine physical and neurological examination, and lastly complete the additional history and inquiry concerning the specific problems presented. It is important that the parents be informed of only that amount of interview material that the patient gives the physician permission to discuss with them: one must prevent the patient from developing the idea that his secret confidences have been revealed. Sometimes the case may be discussed privately with the parents if they are exceptionally reliable.

The taking of a psychiatric type of history is, of course, the preferred way to obtain material; it is also essential to cover the field of personality so that no important traits are overlooked. The particular subjects to be covered are stressed in the following section.

PSYCHIATRIC HISTORY

Persistent *neurotic traits* in children are often early indications of personality deviations. One should therefore question the patient and later the parents concerning bedwetting prolonged after the age of two and temper tantrums, such as episodes of screaming, foot-stamping, breath-holding, assaults on an offending person and destructiveness. The occurrence of these episodes suggests that as a child the adolescent acquired abnormal methods of gaining attention or expressions of sympathy and affection from the parents.

The *day-dreaming and fantasy life*, as well as persistent or vivid night-dreaming, are significant, since they reveal the presence of chronic fear as well as the tendency to withdraw from the practical and real into the attitude of pleasurable and effortless castle-building. This tendency is often the first expression of an introverted or a schizoid personality, and its seriousness is entirely measurable by the amount of time which the adolescent spends in day-dreaming. If along with this activity he shuns physical contacts such as those made in sports, avoids social contacts such as companionships of his age group and prefers to stay by himself and read most of the time, one can conclude that these symptoms of withdrawal are ominous.

Personal ambition, whether practical or impractical, again gives a clue to the personality type as well as to any potential problems of personality. All adolescents go through periods of rather wild ambitions to be famous in a variety of fields of life, and the example of a few famous men in certain fields who from an early age had been obsessed with a desire to follow that particular field makes a proper judgment of an adolescent's choice of goal difficult. For example, given a case in which the adolescent has a strong physique, an extrovert type of personality and a school record showing proficiency in sciences, one would be rather doubtful of his obtaining success in music, particularly if one discovered later in the examination that the father's brother had been a rather well-known musician and that the father had been unconsciously forcing the adolescent in a similar direction. Ambition ideals must be tempered with the practical aspects of the patient's personality

*Instructor in psychiatry, Duke University, Durham, North Carolina; assistant to the Medical Director, Highland Hospital.

†Resident psychiatrist, Highland Hospital.

type and background; otherwise, the next few years for that particular adolescent are sure to be excessively difficult.

An accurate description of the adolescent's *loves and attachments*, if it can possibly be obtained, either from him or from outside sources, is of the utmost significance. The absence of proper balance between his attachments to each parent, and the disproportionate interest or attention granted to him by parents, may indicate the basis of feelings of insecurity and emotional tension which one oftentimes sees at this age. In the early years of adolescence one expects the subject's attachment to his own age group to be rather of the unconscious homosexual type, but during the later years, that is, about the age of sixteen and after, his emotional interest should swing to the opposite sex. Tendencies of aggressive or submissive response to overtures of affection need to be properly judged, for here again disproportion in quality or quantity indicates a deviation from the norm. Sorrows and disappointments, depending on their cause and the way in which the adolescent absorbs them or is crushed by them, often indicate the degree of his emotional maturity. If he is excessively depressed by the cold response of an object of his love or by the thwarting of a particular ambition, one should begin planning therapy to promote emotional toughness and maturity. The reaction to the death of a loved one is occasionally quite abnormal in degree, and in this case one should immediately suspect that the patient has been preoccupied with ideas of death and that he may be a definite suicide risk.

Secret fears and uncertainties can cause such emotional disturbance to the adolescent that his efficiency in schoolwork and proper adjustment at home are seriously impaired. One is often surprised at the variety and often the absurdity, from an adult standpoint, of the thing that the adolescent harbors as a secret fear. Strange ideas concerning his family or personal history spring from some half heard or misinterpreted family gossip, or from a comparison of his own person with an abnormal individual with whom he has come in contact. Some of these ideas may be based on past failures in school, in sports or in social adjustment; magnifying his failures, the adolescent begins to fear that he is abnormal.

Psychic trauma may be either the origin of morbid fears and chronic emotional tension or the precipitating factor of an acute emotional upset. An acutely embarrassing episode in school in which the adolescent is revealed in an unfavorable light to his fellow students, or the occurrence of an expression of fear or cowardice in sports, or the

persistence of excessive criticism by his colleagues of some personal physical defect, may form a psychic trauma of sufficient degree to warp the adolescent's adequate adjustment to himself and to others. The commonest source of psychic trauma is in the sexual field, but the unfulfilled desire to be a hero or an object of appreciation and envy by his fellows is also a frequent cause.

Sexual knowledge or misbeliefs, experiences and fears form a considerable portion of the adolescent's personal problems. In present times the amount of sex education available and the method of obtaining it during adolescence are considerably better than they were in the past, yet there is a great deal to be done before this very important life situation can be correctly and safely handled. Despite the apparently early age at which modern boys and girls become acquainted with sexual matters, it is often amazing to discover the amount of ignorance or more often half ignorance which an adolescent possesses. Because of the excessive attention paid to Freudian concepts from a "popular standpoint," one sees more evidence of a swing of the pendulum in the other direction. One meets discouraging resistance from parents and educators in matters of sex education, and this further suggests that the family physician is much better fitted and in a much better emotional position than the parents or educators to give this information to adolescents. Careful questioning of adolescents often reveals that their seemingly flippant and voluminous acquaintance with sexual topics is nothing but a veneer under which there is considerable uncertainty and a definite groping for accurate information. One has only to have as patients a few adolescents who have been the objects of illegitimate pregnancies, rape, homosexual assaults or venereal disease to realize what tragedies these occurrences can seem to them. On investigating these cases one clearly sees how inadequate is the present amount of sex education that most adolescents receive. It is obvious from occurrences like these that the vast proportion of sexual information is obtained from half-truths described or demonstrated by other adolescents and by vulgar minded adults. Masturbation has been investigated and described for enough years to be properly understood, yet the majority of lay people and a number of physicians still believe that it is a serious physical and moral offense that casts a shadow on the body, mind and soul of the indulger.

Intrafamily relationships properly evaluated are often indicative of an adolescent's degree of maturity. The defects and immaturity of the only child are well known and often exaggerated, but

they are not exaggerated if the particular adolescent is an only child who is overprotected against contacts with contemporaries. If the only child is permitted to mix with his age group and take the average knocks from his environment, he need not differ in degree of maturity from the adolescent who is one of several siblings. Family relationships that are modified or marred by an excessively dominant parent, by an only child or by a favorite child, may produce in the adolescent's personality definite traits of inadequacy and feelings of inferiority; similar effects are seen when the affection and economic generosity of the parents have been unequally distributed among the children.

The presence of any *symptoms of a psychosis* should be confirmed. Remembering that the early years of adolescence are accompanied by spells of moodiness, vague longings, incompletely formulated desires and ambitions, and short periods of mild restlessness, one can then look for exaggeration of these phenomena and for other abnormalities. Does the adolescent describe difficulty in concentrating or in thinking? Does he feel a sense of strangeness or remoteness within himself? Do his surroundings and the people about him appear unreal? Does he feel that others, including strangers, make fun of him by word or gesture or talk among themselves concerning him? Has he noticed any peculiarity of traits or gestures in those around him to suggest that these have special meaning to him? When alone or at a distance from others has he heard them talking about him, calling his name, making derogatory remarks about him or labeling him with obscene terms? Has he been in strangely close relations with God, either by some sign in his environment or by hearing God's voice? Has his physical appearance changed strikingly in size, contour, color or sex, or has either half of his body assumed a dominant value? In addition, the physician should note in the patient's general appearance and behavior whether he is unduly restless, fearful, suspicious, irritable, silly, manneristic, emotionally flattened and withdrawn, or unresponsive. He should obtain from the relatives a description of the patient's usual conduct or change in conduct, particularly whether he keeps to himself excessively, is careless or excessively careful or fantastic in his personal appearance and personal hygiene, talks to himself, makes odd gestures, shows emotional outbursts or indulges in silly smiling or laughing without adequate cause, seems perplexed, confused or retarded, or, in general, acts or appears strange compared with his colleagues.

ESTIMATION OF THE CASE

First must be considered the acute problem which brought the adolescent to the physician. It

may be an unexpected failure in school, or a sudden rebellion against authority, whether parental, religious or civic. Oftentimes it is caused by sexual transgressions, either masturbation or the occurrence of homosexual or heterosexual activity with a playmate. The problem may be the continuance or reappearance of some childhood neurotic trait such as bedwetting or temper tantrums that the long-suffering parents have finally but rather tardily decided needs scientific care. A clash with a sibling or a schoolmate may have resulted in a rather vicious physical reaction, such as assaultiveness or destructiveness. Dishonesty, either lying or stealing, frequently causes the parents to bring the adolescent to the physician for help.

The acute problem is often relatively superficial and only a mask hiding a much more serious, more deep-seated and more prolonged maladjustment that might be termed a chronic problem. In these cases one finds sibling rivalry, resentment or overprotection by parents, depression and uneasiness from guilty feelings concerning masturbation, or unacceptable feelings of physical inferiority in competition with playmates. Perhaps a dislocation of family setting is preying on the adolescent as he finds himself emotionally torn between allegiance to a natural parent and love for a foster or a divorced parent.

Evaluation of the personality type of the patient is possible at this stage of psychiatric examination. By putting together the material obtained from the parents and from the patient and that gained by one's own observation one can accurately classify the personality type as introverted, extroverted, emotionally mature or immature. Subtypes could be included but their inclusion would excessively complicate the procedure from a descriptive, and particularly from a general therapeutic, standpoint. At this stage, too, one must approximate the intellectual capacity of the adolescent, since it is obvious that with a subnormal intellect his maladjustment may be entirely on the basis of bewilderment secondary to demands made on him by family pride and by environment. The labeling of an adolescent as a true psychopath is a serious matter and cannot safely be done by anyone not skilled in psychiatry. The history, physical examination, neurological examination and psychiatric examination may elicit sufficient material to make one suspect a psychosis or a psychopathic state such as postencephalitic behavior disturbance, post-traumatic behavior disturbance, mental deficiency or epileptic phenomena, such as petit-mal attacks, psychic equivalents and automatism.

An appreciable amount of moodiness, poetry writing, abstract philosophizing, chronic cynicism, extreme sympathy for the underdog and so forth

are all quite normal during puberty and adolescence. A tendency to leftist leanings is common in the late period of adolescence and is well demonstrated by the noisy behavior of student groups. The following poems² are excellent examples of an adolescent's mental gropings for and understanding of herself, and her environment and the relation of herself to the latter. The authoress was fourteen at the time she wrote the first and seven teen at the time of writing the second.

DEATH MOOD

Is death but a sleeping
From which there is no waking
A night without a dawn?
Is sleep a taste of dying,
An oblivion of dream-eternity?

What happens in those lethal moments?
Years pass between each living day
Of which we are unmindful
Until slow creeping Time
Has found us with his cobwebs,
Has bound us with his cobwebs,
Has dragged us to his dungeon
There to shrivel up and die!

Is life but a searching,
A questioning and searching
A weary futile seeking
For non-existent things?
Is death then the answer,
Is death or God the answer
To the helplessness, the hopefulness,
The beating of our wings?

DEATH MOOD (LATER)

I

Since you must seek me out, oh, peaceful death,
I pray that you will come on velvet feet
Into my weary heart and, for a breath,
Feel its glad welcome in a quickened beat
Or, as I lie upon these sunlit sands,
Beckon to me across the ocean wave
That I may swim to your outstretching hands,
Rather than join you in some earthy grave
But spare me an oblivion too deep
Until I write a final brief farewell
To my few friends. Then as I fall asleep,

Let the bewitching solo of a bell
That I have often held my breath to hear
Sound its enchanting music in my ear

II

Since I must die, I ask that death may be
A quick ecstatic moment when it comes
I do not wish to feel security
Slip from me slowly, nor the peace that numbs
Quiet my throbbing pulse. No chair for me
On a sunny lawn and a nap at noon!
I have pursued a life so bold and free
Rather than creeping age let death come soon!—
A dagger thrust that swiftly finds its mark,
A sudden leap into a rushing stream
Or stumbling footsteps on a cliff at dark
Would capture death outside some tortured dream,
Nor let me falter at the black void's brim,
Fearing what may be seen beyond the rim!

(Four additional stanzas follow)

CONCLUSION

A practical mode of psychiatric investigation applicable to handling the problems of adolescence is outlined, and a brief explanation of the various etiologic factors met with in such cases is made. This age group of patients, with the clinical picture peculiar to them, forms a segment of potential patients who merit the serious attention of the general practitioner. By the application of the principles of mental hygiene not only can the family physician help some of these boys and girls over difficult spots during their adolescent years, but he can very frequently abort any tendency to the development of a neurosis, psychosis or warped personality. When he is giving periodic care to the children, the alert family physician can suggest to the parents that at puberty these young people be referred to him for definite sex education, and that during the later years of adolescence they again seek his counsel on other problems of personality adjustment.

REFERENCE

- 1 Sullivan D. J. and Flanagan N. B. Practical psychotherapy with adolescents: a brief survey of the field for the general practitioner. *New Eng. J. Med.* 221:414-419, 1939.
- 2 Schaeffle E. *Veres*. 63 pp. New York: Henry Harrisson, 1938.

AN EXPERIMENTAL STUDY OF THE TREATMENT OF AIR EMBOLISM*

JACOB FINE, M.D.,† AND JOSEPH FISCHMANN, M.D.‡

BOSTON

THE increasing usefulness of air as a contrast medium in radiological diagnosis requires adequate preparation to deal with the one major catastrophe which may result, namely, air embolism. Circulatory occlusion by air may be disastrous in three ways: by obstructing a sufficiently large area of the pulmonary capillary bed to interfere with the transfer of an adequate volume of oxygenated blood from the right ventricle to the left auricle; by obstructing one or more branches of the coronary arteries; or by rendering ischemic a vital area in the brain. If death does not result at once, the outcome will depend on the function of the involved area and the length of time it can tolerate ischemia. Since time is of the greatest importance, immediate steps to absorb the nitrogen must be undertaken to mitigate the serious effects which not infrequently cause death later. In several publications¹⁻⁵ from this clinic, experimental and clinical evidence was provided to show that the absorption of nitrogen from the body tissues is facilitated by the inhalation of 95 to 100 per cent oxygen. The application of this agent was recommended among other things for the treatment of air embolism,⁵ although no clinical opportunity to test such a situation had presented itself. Meanwhile, clinical accounts of air embolism continue to be published,^{6, 7} which demonstrate the helplessness of the physician in such accidents, although the present practice of decompressing divers with oxygen, as suggested by Behnke et al.,⁸ should provide a broad hint as to what to do.

To re-emphasize the value of immediately applying pure-oxygen inhalations for air embolism, we have carried out a series of simple experiments on rabbits, instead of waiting for a personal clinical experience to demonstrate its effectiveness.

METHOD

The right or left carotid artery of 9 rabbits was exposed under ether anesthesia. Three to 5 cc. of blood was withdrawn, mixed by shaking with 1 cc. of air and reintroduced into the artery. The artery was then ligated to prevent bleeding, and the wound was closed. In nearly every experi-

ment a tetanic spasm of the entire musculature of the body resulted immediately, but invariably recovery occurred promptly. In Experiment 3 (Table 1), immediate death resulted because the air was insufficiently dispersed into tiny bubbles during the mixing with blood. On recovery from the anesthesia, paralysis of one or more muscles in one or more extremities was observed, and the length of time for return of normal function was noted.

A second series of 13 rabbits was treated and observed in similar fashion, except that immediately following the air injection the rabbit was placed in an oxygen chamber (90 to 100 per cent concentration), in most cases for one or two hours. The first two rabbits, exposed for three and eight hours respectively, succumbed to pulmonary edema caused by the intolerance of rabbits to high concentrations of oxygen for more than one-hour or two-hour periods.

RESULTS

Damage to muscular function of the extremities occurred in all but 2 of the 21 animals surviving the air injection. The determination of the extent of muscular paresis was possible only after recovery from ether anesthesia, except in Experiments 20, 21 and 22, in which local anesthesia was used. Since there were no simple objective signs of air embolism except muscular paresis, we utilized this as a measure of the extent and duration of injury caused by the air embolus for the purpose of evaluating the therapeutic effect of breathing pure oxygen.

Table 1 demonstrates clearly the considerable advantage that oxygen provides. The 8 surviving rabbits in the control series required an average of *eleven days* for full recovery from muscular paresis. In contrast, 10 of the 11 rabbits that showed muscular weakness and were given oxygen inhalations required an average of less than *ten hours* for full recovery of function. In the eleventh rabbit (Experiment 22) oxygen was apparently of no benefit, and death resulted on the fifth day. The data in the "Comment" column of the table include details that emphasize the sharp difference in the course of events induced by the oxygen inhalations.

The two rabbits that showed no apparent injury following the air injection (Experiments 16 and

*From the Surgical Laboratory, Beth Israel Hospital, and the Department of Surgery, Harvard Medical School.

†Associate in surgery, Harvard Medical School; visiting surgeon, Beth Israel Hospital.

‡Research fellow in surgery, Harvard Medical School.

TABLE 1. *Data on Rabbits.*

EXPERIMENT NO.	CAROTID ARTERY INJECTED	IMMEDIATE EFFECT OF AIR EMBOLISM	TIME REQUIRED FOR FULL RECOVERY	COMMENT
CONTROL SERIES				
1	Right	Marked paralysis of all extremities	10 days	1 cc blood mixed with 1 cc air hindlegs normal after 48 hours left foreleg normal on 5th day, extensor paralysis of right foreleg last to disappear
2	Right	Extensor paralysis of right fore leg	13 days	2 cc blood mixed with 0.75 cc air no substantial change for 12 days
3	Right	Immediate death	—	3 cc blood and 1 cc of air, poorly mixed
4	Right	Severe paralysis of all extremities	14 days	Slight improvement in all legs on 3rd day but could not jump or sit up, hindlegs normal and right foreleg slightly improved on 8th day, extensor of left foreleg still slightly paretic on 12th day
5	Right	Extensor paralysis of right fore leg	5 days	Improvement not evident until 4th day
6	Right	Extensor paralysis of both fore legs	12 days	Left foreleg normal after 24 hours some improvement of right foreleg on 8th day
7	Right	Complete paralysis of all four legs	13 days	Both left limbs improved on 3rd day and almost normal on 6th on 8th day only right foreleg extensor paretic
8	Left	Complete paralysis of right hindleg moderate paralysis of both forelegs	12 days	Slight improvement of both forelegs after 24 hours right foreleg normal on 4th day, both forelegs normal on 7th day
9	Left	Paralysis of all four legs most marked in left foreleg	7 days	Hindlegs improved within 24 hours and normal on 4th day extensor of left foreleg still markedly paretic until 6th day
OXYGEN SERIES				
10	Right	Extensor paralysis of right fore leg	4–16 hr	Breathed pure oxygen for 8 hours death on 3rd day with edema of right lung and right hemothorax extensor paralysis showed improvement after 4 hours in oxygen tent and was entirely absent when observed the following morning
11	Right	Extensor paralysis of right fore leg	5½ hr	Breathed pure oxygen for 3½ hours removed from oxygen because of increasing dyspnea no paralysis 2 hours later but progressive dyspnea and death in 22 hours autopsy showed bilateral pneumonia wet lung* and trabecular hemorrhage
12	Right	Marked paralysis of all four legs completely immobilized	3¼ hr	Removed from oxygen tent after 2 hours ½ hour later showed marked improvement, jumped about without disability 3¼ hours after air injection
13	Right	Severe extensor paralysis of left foreleg and slight paralysis of left hindleg	2–18 hr	Marked improvement of left foreleg and complete recovery of left hindleg within 2 hours after air injection fully recovered following morning
14	Right	Slight paralysis of both fore legs	1–17 hr	Left foreleg normal jumped and sat up well within 1 hour after air injection
15	Left	Slight weakness of right fore leg	1½ hr	
16	Right	No effect	—	
17	Right	Marked paralysis of right fore leg	3–20 hr	Recovery almost complete 3 hours after air injection, complete next morning
18	Left	Slight paralysis of right fore leg	2 hr	Recovery almost complete after 2 hours death in 17 hours autopsy showed hemothorax
19	Right	No effect	—	Showed no tetanic spasm after injection
20	Right	Marked paralysis of both fore legs	2–18 hr	Experiment under local instead of ether anesthesia given 100 per cent oxygen by tracheal cannula for ½ hour preceding air injection, typical convulsive seizure and paralysis left foreleg normal after breathing pure oxygen for 2 hours right foreleg still a bit weak but normal following morning
21	Right	Complete paralysis of all extremities and of posterior neck muscles	—	Experiment under local instead of ether anesthesia given 100 per cent oxygen by cannula for ½ hour before and 1 hour after air embolism 5 hours later hindlegs slightly improved much better after 48 hours, but paralysis complete in right foreleg and severe in left foreleg on 4th day died on 5th day of pneumonia and basilar meningitis
22	Right	Severe paralysis of all four legs	24–42 hr	Experiment under local anesthesia given 100 per cent oxygen by tracheal cannula for ½ hour before and 1 hour after air injection within 2 hours left foreleg and hindlegs normal, after 5 hours only extensor paralysis of right foreleg after 24 hours very slight weakness of right foreleg which was normal the following morning

19) were among those given oxygen immediately after the air injection. One of these showed the characteristic convulsive spasm observed immediately following the injection of air into the carotid artery. In this case the failure of muscle weakness to appear might have been due to an unusually rapid absorption of the nitrogen by the oxygen inhalations. In the other case, however, a convulsive seizure did not follow the air injection, so that the absence of muscle weakness on recovery from the anesthetic cannot be considered a result of the administration of the oxygen.

In Experiments 20, 21 and 22, 100 per cent oxygen was given by tracheal cannula for half an hour prior to producing the air embolus in order to test the prophylactic value of this agent. All animals developed muscular paresis. The prophylactic value of oxygen was not demonstrated, since the time for full recovery in the 2 surviving rabbits (Experiments 20 and 22) was not less than that for the rest of the group, in spite of the additional inhalation of oxygen following the air injection. This observation is in agreement with that from a similar study previously made in cats, in which no protection against air injected intravenously was afforded by a preliminary period of breathing pure oxygen.¹

DISCUSSION

The time required for a bubble of nitrogen blocking a cerebral vessel to diffuse out of the blood stream into the expired air while 100 per cent oxygen is being breathed depends on the size of the bubble, but it is probably completely disposed of within the time of exposure to oxygen utilized in these experiments.¹ It was not possible to determine whether the time for recovery of function might have been shortened still further by a longer exposure to oxygen, because of the intolerance of rabbits to longer exposures. The relatively long duration of the paresis as compared with the short time of exposure to oxygen is clearly due to the long period of recovery required by the injured nerve cells. The more rapid recovery of function by the nerve cells of the rabbits that were given oxygen is not adequately explained on the basis of a greater oxygen saturation of the brain, for the oxygen deficit produced by the air embolus is probably far greater than can be compensated for by an increase in diffusion of oxygen from neighboring tissues. The mechanism of the action of oxygen in these circumstances is therefore, in our view, that referred to in a preceding publication⁹: that is, the inhalation of pure oxygen necessarily and rapidly reduces the pressure of nitrogen in the lungs toward zero, so that nitrogen in the blood,

which is then at a relatively much higher pressure, must, according to Henry's law, diffuse into the expired air.

The technic of the procedure in these experiments included ligation of the carotid artery following air injection. This was found necessary because the needle-puncture wound tended to bleed in spite of pressure for several minutes. Ligation of one carotid artery in the rabbit does not cause muscular paralysis. It therefore cannot be of consequence in evaluating the benefit of the oxygen, since the same technic was applied to both series of animals.

The failure to observe any benefit from the inhalation of 100 per cent oxygen in advance of the production of the air embolus is presumably due to the fact that the flow of nitrogen from the blood stream to the alveolar air is rapidly slowed because of the immediate rise in the partial pressure of nitrogen in the lungs as soon as the first breath of air replaces that of pure oxygen.

The use of 100 per cent oxygen for the treatment of human cases of air embolus cannot be expected to show the remarkably uniform success obtained in these experiments, even if applied without delay at the instant air embolism occurs. This should be obvious from the fact that much depends on the volume of the air embolus. The amount of air which can be tolerated without serious consequences by the pulmonary capillary bed is obviously much greater than it is in the brain or the coronary arteries. The entrance of air into the latter is not likely except in the case of a patent foramen ovale or when, during a thoracic procedure, air enters a tributary of a pulmonary vein. Although air may reach the brain under similar circumstances, an alternative route of cerebral air embolism may be that recently demonstrated by Batson,¹⁰ that is, the vertebral venous plexus, which by virtue of its rich anastomosis with the tributaries of the vena cava and azygos veins may act as a by-pass of the systemic venous circulation. By this route, however, obstruction of the cerebral circulation by air would require the existence of arteriovenous anastomoses, the evidence for which is equivocal.¹¹ On theoretical grounds a high degree of success should attend the use of 100 per cent oxygen inhalation when small emboli reach the coronary arteries or the brain. Even a large embolus, if not immediately fatal, might be absorbed in time to avert permanent damage or subsequent death.

The substitution of oxygen for air as a visualizing agent does not prevent the adverse effects of gases in body tissues or cavities.¹ This observation

has recently been confirmed by Moore and Braxton.¹²

The very rapid ascent into high altitudes by military aviators using interceptor planes is said to produce symptoms due to the liberation of free nitrogen in the blood stream. The evidence from these experiments and previous publications^{1, 2, 3, 8} indicates that such symptoms can be minimized or avoided altogether by pre-oxygenation with 100 per cent oxygen and by the continued inhalation of 100 per cent oxygen during ascent. Pre-oxygenation would remove the nitrogen dissolved in the blood stream, and the continued inhalation of oxygen during ascent would cause the nitrogen entering the blood stream from the tissues to escape via the lungs without forming gaseous emboli.

CONCLUSIONS

In rabbits the serious effects of an air embolism that was not immediately fatal were prevented or rapidly alleviated by the prompt administration for several hours of 100 per cent oxygen inhalations. This procedure may be of significance in the treatment of certain types of human cases.

In rabbits the use of 100 per cent oxygen in-

halations as a prophylactic agent against air embolism had no beneficial effect. The same would probably hold true in patients when air is injected for diagnostic purposes.

330 Brookline Avenue

REFERENCES

- 1 Fine J, Frehling S and Starr A. Experimental observations on the effect of 95 per cent oxygen on the absorption of air from the body tissues. *J Thoracic Surg* 4:635-642 1935
- 2 Fine J, Sears J B and Banks B M. The effect of oxygen inhalation on gaseous distention of the stomach and small intestine. *Am J Digest Dis & Nutrition* 2:361-367 1935
- 3 Fine J, Banks B M and Hermanson L. The treatment of gaseous distention of the intestine by the inhalation of 95 per cent oxygen. *Ann Surg* 103:353-387 1936
- 4 Schwab R, Fine J and Mixer W J. The reduction of postencephalographic symptoms by the inhalation of 95 per cent oxygen. *Arch Neurol & Psychiat* 37:121-128 1937
- 5 Fine J, Hermanson L, and Frehling S. Further clinical experiments with 95 per cent oxygen for the absorption of air from the body tissues. *Ann Surg* 107:113-138 1938
- 6 Weyrauch H M Jr. Death from a r embolism following perirenal insufflation. *J A M A* 114:652-1940
- 7 Walsh F B and Goldberg H K. Blindness due to air embolism: a complication of extrapleural pneumolysis. *J A M A* 114:654, 1940
- 8 Behnke A R, Shaw L A, Messer A G, Thompson R M and Moley E P. Circulatory and respiratory disturbances of acute compressed air illness and the administration of oxygen as a therapeutic measure. *Am J Physiol* 114:526-533 1936
- 9 Rosenfeld L and Fine J. The effect of breathing 95 per cent oxygen upon intraluminal pressure occurs even by gaseous distention of obstructed small intestine. *Ann Surg* 108:1012-1021 1938
- 10 Batson O V. The function of the vertebral veins and the role in the spread of metastases. *Ann Surg* 112:138-149 1940
- 11 Cobb S and Alexander, L. personal communication
- 12 Moore R M and Braxton C W Jr. Injections of air and of carbon dioxide into a pulmonary vein. *Ann Surg* 112:212-218 1940

GLOMUS TUMOR

Report of a Case

RUDOLPH E SWENSON, M.D.*

PLYMOUTH, MASSACHUSETTS

TUMORS of the glomus^{1, 2} or arteriovenous anastomosis of the cutis are rare, but are striking because of their symptomatology—chiefly intense pain on pressure and a satisfactory response on local excision. The tumors are usually single, rarely multiple³ and always benign. One of the frequent locations is beneath the nails. A fairly typical case is reported below.

CASE REPORT

An unmarried, white, 28 year-old French Canadian woman was seen on November 5, 1938, complaining of having been tired and sleepy for the last 2 years and of having lost interest in people and in life in general. She stated that 2 years previously she had had a nervous breakdown, which she attributed to overwork.

When questioned as to how she rested at night, she admitted that she was awakened several times by severe pain in the middle finger of the left hand, initiated by the slightest pressure or motion during sleep. During the day, she had to perform her work with four fingers of the left hand while she kept the middle finger extended to avoid the slightest jarring or pressure. Any rather severe blow or squeeze caused extreme pain, mostly in the

terminal phalanx, but also radiating up the left hand and forearm.

The patient was not interested in the finger, but insisted that she had come for a tonic. She believed that nothing could be done for the finger, since many doctors during the previous 15 years had attempted to make a diagnosis and treat the condition, without success. X-ray examination had been negative. Her case had been thoroughly studied in large cities of New England, and at one time she had obtained partial relief from pain by alcohol injection at the base of the affected finger.

She was told that the painful finger was the cause of her fatigue, nervousness and pessimistic attitude toward life. Physical examination was entirely negative except for the exquisitely tender finger. By pressure with a blunt probe tenderness could be shown to be limited to an area about 5 mm in diameter on the palmar side of the terminal phalanx. There was no visible swelling or redness, and nothing could be felt superficially on palpation. Pain and tenderness would not permit firm palpation, which might have revealed a small mass below the fat pad.

The symptoms were so suggestive of glomus tumor that, even in the absence of demonstrable tumor, exploration of the finger was advised. This was done under procain anesthesia on November 19, 1938, at Jordan Hospital, Plymouth, Massachusetts. Below the fat pad, lying almost on the anterior surface of the bone, a firm, spherical tu-

*Staff member, Jordan Hospital.

mor mass 4 mm. in diameter was carefully dissected so that a fine blood vessel of entry at the proximal pole and a similar vessel at the distal pole were demonstrated. Very fine nerve fibrils were seen to spread out toward the tumor. The blood vessels of entry and exit were tied off with fine catgut, and the tumor excised.

The next day, the patient stated that the soreness from the incision was not nearly so bad as the previous pain and tenderness that she had endured almost every day for the preceding 15 years.

The pathological description by Dr. Shields Warren was as follows:

A roughly spherical, brown, moderately firm piece of tissue about 0.4 cm. in diameter. Section shows a discrete tumor partly surrounded by a fibro-fatty cap-



FIGURE 1. Section of Glomus Tumor.

sule. There are several myelinated nerves and arteries in the capsule. There are also nerves forming part of the walls of vascular sinuses. The tumor proper is composed of quite discrete clumps of epithelial-like cells. These cells are compactly arranged and characterized by medium-sized finely granular, round to oval nuclei and indefinitely outlined cytoplasm that appears to merge with that of neighboring cells, forming a syncytium. In some of these cell masses there are elongated nuclei lying in a bed of finely fibrillary tissue. These structures resemble nonmyelinated nerve fibers and merge imperceptibly with the matrix in which the cell groups lie. This matrix is in part a fine fibrillary substance and in part a homogenous-staining

hyalin-like substance, in which may be seen sparsely scattered slender oval nuclei, vascular channels lined by endothelium and often without a definite wall, non-myelinated nerves and foci of myxomatous degeneration. The most interesting feature of this matrix substance is the close association of nerves and vascular channels, which, as noted in the capsule, are often united so that the nerve appears to form an essential part of the wall of the artery. Diagnosis: glomus tumor.

The patient has had no recurrence of pain or tenderness. Her outlook on life has become quite cheerful, and she is energetic and in the best of health. She was married in July, 1940.

Even though glomus tumor is rather rare, the importance of its recognition by the medical profession is obvious. Some patients, after years of torture, have contemplated suicide. Their suffering can have a profound effect on their lives. They have been given diagnoses of neuritis, neuralgia or neurasthenia.

Glomus tumor is a vascular tumor composed of a varying amount of epithelial or fibrous tissue and very sensitive nerve endings or of a characteristic blending of nerve tissue in vascular tissue. It is usually quite small, 2 to 10 mm. in diameter, and is found subungually in the extremities or subcutaneously over various parts of the body. Under the nail or under the skin it appears as a reddish-blue spot. Excruciating pain caused by the lightest pressure is the characteristic symptom. Glomus tumor has been descriptively called neuroangio-fibroma.

SUMMARY

A case of glomus tumor is reported which was unusual in its location and in that, except for extreme tenderness, no physical signs of its presence could be ascertained before operation.

1 Carver Street

REFERENCES

1. Bailey, O. T.: Cutaneous glomus and its tumors — glomangiomas. *Am. J. Path.* 11:915-936, 1935.
2. Stout, A. P.: Tumors of neuromyoarterial glomus. *Am. J. Cancer* 24:255-272, 1935.
3. Weidman, F. D., and Wise, F.: Multiple glomus tumors of order of telangiectases. *Arch. Dermat. & Syph.* 35:414-426, 1937.

REPORT ON MEDICAL PROGRESS

CLINICAL AND EXPERIMENTAL EVIDENCE ON THE NUTRITIONAL REQUIREMENTS IN OBSTRUCTIVE JAUNDICE*

JOHN D. STEWART, M.D.†

BOSTON

OWING to advances in preoperative and postoperative care, it has become possible to perform remedial or palliative surgical operations on desperately sick jaundiced patients without undue risk. Recent biochemical studies have thrown light on some of the complicated metabolic errors that occur in obstructive jaundice and other forms of liver disease. As the nature of the hepatic impairment comes into clearer focus, preoperative needs grow less obscure, and the cause of grave postoperative complications may be corrected. An impressive illustration is the discovery of vitamin K and the solution of the problem of the dangerous bleeding tendency in obstructive jaundice, an achievement dependent on the joint efforts of biochemists and alert clinicians. Recognition of the clinical fruitfulness of knowledge gained in biochemical and physiological studies leads the resourceful clinician to give attention to the teachings of the laboratory.

For over sixty years it has been known that the hepatic glycogen content falls in animals exposed to such poisons as chloroform, arsenic and phosphorus, and that simultaneous increase in hepatic lipid occurs. Such observations led to studies of the effect of diet on hepatic reserve and on hepatic composition. Various investigators have shown that preliminary feeding of carbohydrate reduces the susceptibility of animals to hepatotoxic agents, whereas feeding of fat has the opposite effect.¹⁻⁵ Opie and Alford² found, for example, that three times the oral dose of chloroform fatal for white rats receiving a fat diet is tolerated by animals on a meat diet, whereas five times this dose may be safely given to animals that have been fed on starch and sugar. The protective effects of high-carbohydrate feeding and the harmful effects of dietary fat have been shown to hold in the presence of hepatic trauma produced in various ways, as by ligation of the common duct, subtotal hepatectomy, formation of an Eck fistula and production of biliary cirrhosis by cholecystenterostomy.^{6,7}

The manner in which abundant glycogen stores

protect the liver from noxious agents has been the subject of considerable speculation. Rosenfeld,¹ noting the reciprocal relation between stores of glycogen and fat in the liver under a variety of conditions, concluded that fat transported to the liver accumulates there as a secondary phenomenon in the absence of sufficient carbohydrate for its combustion. In his view lack of glycogen is the controlling factor, for without a supply of readily available fuel, the detoxifying and reparative functions of the liver are crippled. There appears to be no evidence, however, that the oxidative processes of hepatic tissue undergo an increase in poisoning. Wells⁸ suggested that hepatic glycogen by its antiketonic action tends to maintain cell neutrality, thus preventing acidosis and degeneration of hepatic tissue. Opie and Alford^{2,3} favor the hypothesis that a high-carbohydrate intake protects against fat-soluble hepatotoxins, such as chloroform and carbon tetrachloride, by minimizing the deposition of fat in hepatic and renal parenchyma, with a consequent reduction in the amount of the toxin taken up by the tissue. The following experimental observations indicate the fact that the nutritional state of the liver and resistance to hepatic trauma are less simply related than this hypothesis suggests. A high-carbohydrate diet is protective in hepatic trauma produced by ligation of the common duct and subtotal hepatectomy; a high-protein intake protects against chloroform poisoning even when hepatic fat content is high⁹; the effects of phosphorus poisoning are heightened in rats by a meat diet rather than fat.²

The well-known protein-sparing action of carbohydrate has been invoked to explain the protection that abundant hepatic glycogen stores afford against hepatic injury. In studying this question Davis, Hall and Whipple¹⁰ obtained convincing evidence of such action in chloroform poisoning after the animals had been fed carbohydrate heavily. They concluded that there is a true conservation of split products of hepatic protein, and that an abundance of glycogen leads to resynthesis of partially disintegrated protein from its original elements. In other words, protein-sparing occurs not at its source, but as conservation of protein end products. The work of Smith and Moise¹¹ on

*From the Surgical Laboratories of the Harvard Medical School at the Massachusetts General Hospital.

†Associate in surgery, Harvard Medical School; assistant surgeon, Massachusetts General Hospital.

the regeneration of liver tissue after chloroform poisoning yielded data consistent with this interpretation. Further study is needed on the relation between the chemical composition of the liver and its vulnerability if this important question is to be elucidated. Such investigation must take note of differences in response of different species, the role of accessory food factors as well as the cardinal foodstuffs, variations in defense reactions to different kinds of poisons and to mechanical trauma or infection, and the possible significance of renal function in influencing hepatic resistance. The distinction between degeneration and repair should be kept in mind, for the ability of hepatic tissue to withstand a single trauma may not parallel its power to heal.

In view of the necessity of conserving the hepatic glycogen stores, studies of the effects of hepatic disease on glycogenesis and glycogenolysis are of great interest. The work of Mann¹² and Soskin¹³ has made it clear that the liver is the sole source of the glucose in the blood. Under physiologic conditions the concentration of glucose in the blood is stabilized by the liver, and an increased intake of glucose leads to glycogen formation and storage, whereas depression of the blood-glucose content is combated by glycogenolysis and liberation of glucose from the liver. The sensitivity of this vital homeostatic mechanism is impaired by hepatotoxins in the experimental animal,¹⁴⁻¹⁶ and by chronic hepatic disease in man.¹⁷⁻²⁰ Disturbances in glycogenesis, glycogenolysis and gluconeogenesis may result. Although higher concentrations of glucose in the blood may be necessary to effect hepatic glycogen storage, the damaged liver is usually still capable of glycogenesis.²¹ The evidence indicates that disturbances in hepatic function leading to hepatic insufficiency may be accompanied by high, low or abnormally labile blood-sugar values, but that glycogen storage in the disabled liver still occurs if sufficient quantities of carbohydrate are taken.

Whether glycogen deposition in the disabled liver proceeds more rapidly when glucose is given by vein than when sufficient carbohydrate is taken by mouth is an unsettled question.²² The intravenous administration of glucose solution provides a strong immediate stimulus to glycogenesis, and often makes it possible to give larger amounts of glucose than the sick patient can take as carbohydrate by mouth. It is true that hypertonic glucose solution must generally be used. The consensus opposes the use of insulin during intravenous glucose therapy in the nondiabetic patient, and as Soskin and Hyman²³ point out, insulin may even be harmful. The injection of insulin,

according to them, causes increased storage of glycogen in the muscles, but without corresponding increase in the liver. Such peripheral glycogen formation tends to lower blood-glucose concentration and thus to reduce the stimulus to hepatic glycogenesis.

Demonstration of the beneficial effects of high-carbohydrate intake in the experimental liver disease of animals has led to the clinical application of carbohydrate therapy in liver disease, with gratifying results. Jones²⁴ was able to show a sharp reduction in the mortality rate in patients with acute hepatic insufficiency after the introduction of intravenous glucose therapy and a high-carbohydrate diet. He concluded that the more intensive the intravenous glucose therapy the better the prognosis. Ravdin and his co-workers²⁵ found that the postoperative mortality rate in patients with obstructive jaundice was cut in half with the routine administration of glucose intravenously before and after operation. Later Ravdin²⁶ expressed some skepticism as to the practical value of intravenous glucose therapy and stressed the use of a high-protein, high-carbohydrate diet in preparing the patient with obstructive jaundice for operation. The value of giving glucose solutions freely by vein in the treatment of liver disease is attested by the experience of various other clinics.^{21, 27, 28}

Increasing experimental evidence points to a relation between the protein stores of the liver and its ability to recuperate from trauma. In work⁹ already referred to it was noted that a high-protein diet produced in rats maximal resistance to chloroform poisoning, regardless of the lipid content of the liver. Miller and Whipple²⁹ observed in dogs an increase in liver damage from chloroform anesthesia as the protein stores were depleted, as by bleeding, plasmapheresis or a low-protein diet. A single large feeding of protein thirty-six hours before chloroform anesthesia seemed to be followed by distinct diminution in the extent of liver damage. Messinger and Hawkins³⁰ found a high-protein diet even more effective than a high-carbohydrate diet in preventing liver damage from arsphenamine. Recently, in a study of dogs with ligated common ducts, maximal glycogen and minimal fat deposition was found³¹ to result from a diet high in protein as well as carbohydrate. Brues, Drury and Brues³² have shown that regeneration of hepatic cells after subtotal hepatectomy proceeds fastest on a high-protein diet, their work being confirmatory of the earlier conclusions of Moise and Smith.³³

In connection with the composition and functional reserve of the liver as influenced by diet, the work of Best and his colleagues^{34, 35} and of

Channon and Wilkinson³⁶ is of great interest. These workers showed that the extreme fatty infiltration of the liver that occurs in depancreatized dogs given insulin could be prevented by feeding lecithin, choline, betaine, casein and other dietary proteins. Dragstedt and his associates³⁷ demonstrated that fatal fatty degeneration and infiltration in the liver could also be prevented by feeding raw pancreas or an alcoholic extract of beef pancreas. The existence of a pancreatic fat-metabolizing hormone was announced, and the new hormone was named "lipocric." MacKay,³⁸ in confirmation of this work, reported that pancreatic extracts made by Dragstedt's method prevented the deposition of fat in the livers of rats fed a diet deficient in choline and other lipotropic elements. Best and Ridout³⁹ have questioned Dragstedt's conclusions, and consider that the lipotropic effect of pancreatic extract is not that of a new specific factor, but is due to the choline and protein content of the extract. In a later report, Dragstedt⁴⁰ seems to have shown that the choline content of the pancreatic extract he produced was entirely too small to explain its lipotropic power.

A large store of protein material is found in the normal liver,⁴¹⁻⁴² and as Whipple points out,⁴³ all the evidence indicates that the liver is of primary importance in protein metabolism. It has been shown⁴⁴ that after a rapid and extreme plasma depletion the dog can throw into the circulating plasma considerable amounts of protein within an hour or two. The presence of an Eck fistula or of severe liver injury abolishes this reaction.⁴⁵ A fall in plasma protein concentration with alteration of the albumin-globulin ratio can be produced in dogs by repeated oral doses of carbon tetrachloride.⁴⁶

It is a common clinical observation⁴⁷⁻⁵⁰ that the plasma protein concentration may be low in various types of hepatic disease, and that the albumin fraction is more often depressed than the globulin fraction. Butt, Snell and Keys¹ showed that determination of total serum protein concentration may fail to disclose sharp disturbances in the serum protein pattern in liver disease, and that the relation between serum protein concentration and colloid osmotic pressure is variable, owing to changes in the albumin-globulin ratio. These authors in studying 15 cases of obstructive jaundice found an average serum protein value of 6.2 gm per 100 cc, an average albumin-globulin ratio of 1.22 and an average serum colloid osmotic pressure of 250 mm of water, the average normal value for the latter being 370 mm. These findings illustrate the point that although the total plasma protein concentration is important, of greater sig-

nificance are changes in colloid osmotic pressure and alterations of the plasma protein pattern.

The implication that such experimental and clinical observations have on the treatment of patients with severe liver disease is clear concerning the great value of transfusions of blood and plasma, but as concerns the indications for a high protein diet the conclusions are less clear cut. It has long been known that dogs with Eck fistulas can be maintained in reasonably good health only if the meat content of the diet is kept low. Opie and Alford² found that phosphorus was more toxic in rats kept on a meat diet than in those kept on a fat diet. Mann⁷ was able to keep dogs with obstructive jaundice, cirrhosis or a surgically reduced hepatic mass in fairly good condition for many months, but on the substitution of meat for carbohydrate in the diet, ascites and liver failure set in. Aqueous meat extracts, free from protein and fat, were even more harmful to hepatic reserve.⁶ Apparently in considering the influence of a high protein diet on the liver, the distinction must be made between protein of meat and of milk, for the experimental evidence from various sources^{6,9,33} indicates that casein has beneficial effects. Although there can be no doubt that feeding casein to the healthy animal increases resistance to experimental hepatic trauma, it still remains to be shown that the damaged liver responds favorably to a high casein intake, and for the clinician this is an important distinction. A reasonable course in the treatment of hepatic disease at present seems to be the inclusion of moderate amounts of protein in the diet, with a preference for the protein of eggs and milk.

The liver in its role as "the commissariat of the body"⁵² plays a leading part in the metabolism of the vitamins, although much remains to be learned about the mechanisms involved. The experimental and clinical evidence turns on such questions as changes in hepatic function and morphology due to vitamin deficiency, interference with vitamin storage in liver disease, failure in absorption of vitamins or their precursor substances and impaired conversion of precursor material into the metabolically useful factor.

György and Goldblatt⁵³ found that rats fed a basal diet lacking in the vitamin B complex and supplemented by thiamin chloride, riboflavin and pyridoxin during the course of four to twelve weeks developed fatal degenerative and necrotic changes in the liver. The hepatic lesions were of the acute and precirrhotic type seen after carbon tetrachloride poisoning, and the changes did not occur if yeast or Peters's eluate was included in the diet. However, the ration used was almost devoid of purine substances, which left the nature of the

nutritional defect uncertain. The authors comment on the chemical and toxicological studies of Neale and Winter,⁵⁴ who offered some evidence suggesting that sodium xanthine and some other related purine derivatives, including guanosine, guanine and hypoxanthine, exhibit protective action against the hepatic lesions due to chloroform or carbon tetrachloride poisoning.

Rich and Hamilton⁵⁵ were able to produce cirrhosis of the liver consistently in rabbits by giving them a basal diet supplemented with various vitamins but lacking yeast. The evidence pointed to the conclusion that the cirrhosis, which was of the human Laennec type, was due to the lack of some factor contained in yeast but different from thiamin chloride, riboflavin, nicotinic acid and pyridoxin. The possibility that lack of choline in the diet may have produced the hepatic changes was not excluded by the experimental data, but as the authors point out, fatty infiltration rather than portal cirrhosis is to be expected from choline deficiency.

In a study of the vitamin A content of hepatic tissue obtained at autopsy in over 1000 cases, Moore⁵⁶ found that cirrhosis of the liver was one of the diseases showing the lowest values. He concluded that the hepatic storehouse may undergo vitamin A depletion in various diseases. Stewart and Rourke⁵⁷ have noted the frequent occurrence of low or even absent vitamin A concentration in the plasma of patients suffering from obstructive jaundice. The concentration of carotenoids was less frequently and less severely reduced, a finding plausibly explained by failure of conversion of the precursor substances in the disabled liver. Depletion of vitamin A in the liver and in the plasma is to be expected when the amount of cholic acid delivered into the gastrointestinal tract is deficient, as in obstructive jaundice or impairment of the synthetic functions of the liver, for the vegetable carotenoid substances as well as vitamin A are fat-soluble. In studying the rate of absorption of vitamin A from the gastrointestinal tract in 21 patients with catarrhal jaundice, Breese and McCoord⁵⁸ demonstrated greatly retarded absorption in 12 patients. The delay in absorption was roughly proportional to the liver damage, as measured by the bromphal test, but not to the degree of bilirubinemia.

Vitamin D, like vitamins A, K and E, is fat-soluble, and reduced absorption from the gastrointestinal tract is to be expected in chronic liver disease, obstructive jaundice and biliary fistula. Skeletal decalcification, based on inadequate absorption of vitamin D and calcium, has long been known as a consequence of prolonged loss of bile

in dogs with biliary fistulas. Greaves and Schmidt⁵⁹ showed that vitamin D is not absorbed from the gastrointestinal tract of rats in the absence of bile salts. McNealy, Shapiro and Melnick,⁶⁰ recognizing the possibility of vitamin D lack in jaundice and erroneously assuming its relation to the bleeding tendency, reported good results from the administration of viosterol in jaundiced patients. Stewart and Rourke⁶¹ found abnormally low plasma vitamin C values in patients with untreated obstructive jaundice, and noted that normal values could be established before operation by giving from 300 to 600 mg. of vitamin C daily.

Good results in the treatment of alcoholic cirrhosis of the liver by nutritional therapy have been reported,^{62, 63} and the value of the vitamin B complex has been stressed. Whether the nutritional defects in these cases are due entirely to an inadequate diet, whether the disease of the liver contributes to the malnutrition and whether the nutritional deficiency favors the development of cirrhosis are questions for further investigation. The study⁶⁵ previously referred to should be noted, in which cirrhosis of the liver closely resembling human portal cirrhosis was produced in rabbits by feeding them a diet adequate except for certain components of the vitamin B complex. Annis and Comfort⁶³ state that increasing clinical experience indicates that the vitamins, especially thiamin and the vitamin B complex, are beneficial in treating diseases of the liver, and they point out that crude liver extract contains thiamin in considerable quantities.

It is a clinically familiar fact that patients with chronic affections of the liver frequently have anemia in the absence of evidence of blood loss. Wintrobe⁶⁴ observed a moderate degree of anemia, mostly macrocytic or normocytic in type, in 37 of 44 cases of cirrhosis, in 32 of 36 cases of primary and metastatic neoplasm of the liver and in 33 of 52 cases of miscellaneous hepatic disorders. He found that the cases of macrocytic anemia responded to intramuscular liver therapy, and concluded that macrocytic anemia results in cases of hepatic disease from an inability to store a necessary hematopoietic principle. Stewart and Rourke⁵⁷ found anemia to be the rule in a series of cases of obstructive jaundice, as did Butt, Snell and Keys.⁶¹ Such findings indicate the possible usefulness of liver extract, iron and blood transfusion in the treatment of chronic liver disease, particularly in relation to preoperative and postoperative care.

During the last ten years the riddle of the clotting defect so common and so dangerous in obstructive jaundice has been solved in its practical aspects, although certain questions concerning the

biochemical relations involved are still unanswered. The work of Roderick,⁶⁶ Dam,^{66, 67} Schonheyder,⁶⁸ Almquist and Stokstad,⁶⁹ Quick, Stanley Brown and Bancroft,⁷⁰ Warner, Brinkhous and Smith¹ and others has shown that the pathologic bleeding tendency in sweet clover disease in cattle, in dietary deficiency in chicks and in obstructive jaundice and biliary fistula in dogs and man is based on deficiency of plasma prothrombin. This substance, essential for the rapid formation of an effective clot, is part of the plasma globulin and is formed in the liver. Its formation in sufficient quantity is conditioned in some manner, as yet unknown, by vitamin K, a substance present in various vegetable and animal fats. Hypoprothrombinemia may result from inadequate absorption of fat, as in lack of biliary or pancreatic secretion, from suppression of the synthetic functions of the liver, from too little absorptive intestinal mucosa or too rapid passage of the chyme through the intestine and possibly from insufficient intake of foods containing vitamin K, although the last is somewhat doubtful. Thus hypoprothrombinemia may occur in various disorders of the gastrointestinal tract, though the commonest cause of prothrombin values in the hemorrhagic range is obstructive jaundice.⁷¹

It has been conclusively shown that prothrombin deficiency can be corrected except in extreme liver failure by the oral administration of crude vitamin K extract and bile salts,⁷²⁻⁷⁴ or by parental administration of 2-methyl-1,4-naphthoquinone and various related chemically pure substances.⁷⁵⁻⁷⁸ Rapidly acting water-soluble derivatives of 2-methyl-1,4-naphthoquinone, such as the sodium bisulfite addition product, are now available, and as with other vitamins a wide margin of safety exists between the effective and the toxic doses. Bile salts do not need to be given when the vitamin K active substance is given subcutaneously or intravenously, and the improvement in prothrombin concentration may last a week after a single injection.⁷⁸

In affections of the liver, as in other diseases in which the administration of vitamins is important, the question of adequate dosage presents itself. It cannot be said that the vitamin requirements in health can be closely defined, and the problem is far more difficult in the variations of disease. So-called "subclinical" vitamin deficiencies are probably prevalent among the supposedly healthy, and do not afford sharp criteria with which the effects of various intake levels can be appraised.^{79, 80}

Various methods of study have been devised to give information on individual vitamin needs. The concentration of vitamin A and its carotenoid pre-

cursors in the plasma can be determined in an application of the reaction described by Carr and Price⁸¹ and others^{82, 83}, or the biophotometric measurement of dark adaptation may be made,⁸⁴ although there is some evidence that there may be little correlation between the vitamin A concentration in the plasma and the biophotometer reading.⁸⁵ Goodhart and Sinclair⁸⁶ studied the concentration of cocarboxylase, the diphosphate ester of thiamin, in the blood by a chemical method and found that it varied directly with the amount of total vitamin B₁ in the blood as shown by a biological method. They⁸⁷ concluded that the cocarboxylase determination can be used clinically to demonstrate vitamin B₁ deficiency, with certain rare exceptions, as when the ability of the tissues to phosphorylate thiamin is diminished, or when the red cell or white cell count is greatly increased, as in polycythemia vera or myeloid leukemia. Thiamin concentration in the urine may be measured,⁸⁸ and evidence has been presented to show that correlation exists between the urinary thiamin values and the state of thiamin nutrition.⁸⁹ Ferrebee⁹⁰ has proposed fluorometric methods for estimating the urinary excretion of riboflavin, convenient and accurate enough, according to him, for clinical use. Progress has recently been reported⁹¹ in the demonstration of pyridoxin (vitamin B₆) deficiency in patients by urinary excretion studies. Methods for the determination of vitamin C in blood and urine have been widely used clinically, and much valuable information has been obtained.⁹² Indirect evidence indicative of vitamin D lack can be obtained by measurements of the concentration of calcium and phosphorus in the plasma and urine, and by skeletal x-ray studies. Vitamin K deficiency may be detected by the determination of plasma prothrombin concentration by the two-stage method of Warner, Brinkhous and Smith¹ or by the simpler method of Quick.⁸³

By means of the clinical application of chemical tests wherever possible not only may vitamin therapy be controlled more effectively in the individual case, but information concerning the vitamin needs in various diseases can be accumulated. Should such laboratory data be lacking in the case at hand, the physician would do well to keep in mind that vitamin deficiencies are often multiple, that there is also need for proper amounts of carbohydrate and protein and that the margin of safety between the effective and toxic dose of vitamins is ample. On such grounds the tendency in treating nutritional deficiency is to give amounts of vitamins that are large compared with the estimated needs in health.⁹⁴

In the care of chronic liver disease, and particularly in forms associated with obstruction to bile flow, the advisability of giving the patient cholic acid derivatives must be considered. The digestion and absorption of fats and fat-soluble substances, such as vitamins A, D, E and K, depend on the presence of proper amounts of bile salts in the intestine.^{95, 96} In addition, it has been shown that the interruption of the normal flow of bile into the intestine retards the absorption of hemoglobin-building constituents.¹³ Ivy and Berman⁹⁷ state that glycogen deposition in the liver may be related to the formation and excretion of bile salts into the intestine. It is to be kept in mind that the amount of cholic acid formed by the damaged liver may be reduced, even though the volume of bile is normal, a finding that has been reported frequently⁹⁸ in studies of fistula bile or bile withdrawn from the common duct through a surgical drainage tube. This fact may impair the value of the common clinical practice of re-feeding fistula bile, and suggests that the cholic acid content of such bile should first be determined.

To be balanced against the improvement in digestion and absorption that may result from the oral administration of bile salts in liver disease are the possible toxic effects on the liver and kidneys. Cholic acid and its derivatives when administered by mouth or intravenously are rapidly and quantitatively excreted in the bile.⁹⁹ After the onset of biliary obstruction, cholic acid appears in the blood and urine. When the acid is administered to an animal with biliary obstruction, much of it can be recovered in the urine and the rest is probably broken down in the liver.⁹⁹⁻¹⁰¹ The intravenous injection of sodium dehydrocholate in animals with a ligated common duct produces in many cases albuminuria and cylindruria, elevation of blood nonprotein nitrogen, reduction in urea clearance and lesions in the renal tubules similar to those of uranium poisoning.¹⁰¹ Whether such experimental observations have any bearing on the impairment of renal function and bile nephrosis of human obstructive jaundice may be open to question, but the evidence deserves consideration. Various cholic acid derivatives have been extensively used in the nutritional treatment of obstructive jaundice without definite evidence of harm,⁶¹ but it is probably a reasonable practice to give these substances only in small doses. In patients with obstructive jaundice and severe liver damage I prefer to correct prothrombin deficiency by giving vitamin K parenterally and to administer bile salts by mouth only after surgical relief of the obstruction.

Disturbances in water balance and in renal func-

tion during the course of hepatic affections require careful clinical consideration. The importance of the liver in buffering sudden changes in the composition of the blood has been pointed out repeatedly.¹⁰²⁻¹⁰⁴ Crandall and Roberts¹⁰⁴ found an immediate increase in whole-blood volume after infusion of 0.9 per cent sodium chloride solution in dogs with Eck fistula, the increase being due entirely to plasma. In the normal dog such increase does not occur. Skelton¹⁰⁵ observed a rapid response of the liver and intestines to anhydremia, though the total amount of water in these tissues is far less than that in the muscles and skin. Dogs with Eck fistula show a prompter diuresis after drinking water, and exhibit a lasting increase in volume of water consumed and in urine volume, an effect possibly dependent on interference with the water-storage function of the liver.¹⁰⁶ The same results were found after chloroform poisoning, but not after ligation of the common duct or splanchnicectomy. In acute hepatic injury from arsphenamine poisoning, extensive changes in the electrolyte content of the plasma and urine may occur. The outstanding findings, as reported by Soffer, Dantes and Sobotka,¹⁰⁷ are decreased concentration of plasma chloride and carbon dioxide combining power, increase in inorganic phosphate and in lactic acid and pronounced hemoconcentration; the urine volume increases, and there is increased excretion of lactic acid and total protein and sharp reduction in the excretion of chloride and inorganic phosphate.

In a patient with hepatic insufficiency, rising plasma nonprotein nitrogen values, oliguria and edema are ominous signs, and as Jones and Eaton¹⁰⁸ have pointed out, spontaneous diuresis is evidence of improvement. A complication that ranks high in the fatal cases of obstructive jaundice is anuria, and this is particularly apt to occur in the early postoperative course.¹⁰⁹ In a careful study of renal function in 16 patients with obstructive jaundice, Elsom¹¹⁰ found signs of renal damage in all, including excessive excretion of casts, epithelial cells and leukocytes. Reduction in urea clearance was present in over half the cases, observations that agree with those of Stewart and Rourke⁶¹ in a similar group of cases. Although no conclusive evidence has been adduced in explanation of the renal lesions so commonly found in obstructive jaundice, the pathological findings are definite and characteristic, and have been likened to the renal lesions in transfusion reaction.¹¹¹ In connection with the care of the patient with obstructive jaundice after surgical release of the obstruction, it should not be forgotten that large amounts of water and electrolytes may be lost by external

drainage. As much as 2 liters of fluid containing as much as 15 gm. of sodium chloride may be lost daily in this way.³⁸

Such evidence points up the need for controlling parenteral fluid therapy as accurately as possible in handling cases of obstructive jaundice, for lowered hepatic and renal reserve and disturbances in plasma protein are important factors in determining the fluid requirements in these cases.

REFERENCES

- Rosenfeld, G. Fettersbildung. *Ergebn d. Physiol (Biochemie)* 2:50-94, 1903.
- Opie, E. L., and Alford, L. B. The influence of diet upon necrosis caused by hepatic and renal poisons. I. Diet and the hepatic lesions of chloroform, phosphorus or alcohol. *J. Exper. Med.* 21:120-1915.
- Idem. The influence of diet on hepatic necrosis and toxicity of chloroform. *J. A. M. A.* 62:895-1914.
- Davis, N. C., and Whipple, G. H. The influence of fasting and various diets on the liver injury effected by chloroform anesthesia. *Arch. Int. Med.* 23:612-634, 1919.
- Graham, E. A.
- Graham, E. A.
- Bollman, J. L.
- Mann, F. C. Physiological and pathological reactions of the liver. *South. M. J.* 31:425-430, 1938.
- Wells, H. G. *Chemical Pathology: Being a discussion of general pathology from the standpoint of the chemical processes involved*. Third edition. 797 pp. Philadelphia and London: W. B. Saunders Co., 1918.
- Goldschmidt, S., Vars, H. M., and Ravdin, I. S. The influence of foodstuffs upon the susceptibility of the liver to injury by chloroform and the probable mechanism of their action. *J. Clin. Invest.* 8:277-289, 1939.
- Davis, N. C., Hall, C. C., and Whipple, G. H. The rapid construction of liver cell protein on a strict carbohydrate diet contrasted with fasting. *Arch. Int. Med.* 23:689-710, 1919.
- Smith, A. H., and Moore, T. S. Diet and tissue growth. II. The regeneration of liver tissue during nutrition on inadequate diets and fasting. *J. Exper. Med.* 40:209-218, 1924.
- Mann, F. C. The effects of complete and of partial removal of the liver. *Medicine* 6:419-511, 1927.
- Soskin, S. Muscle glycogen as a source of blood sugar. *Am. J. Physiol.* 11:382-391, 1927.
- Althausen, T. L., and Thoenes, E. Influence on carbohydrate metabolism of experimentally induced hepatic changes. II. Phosphorus poisoning. *Arch. Int. Med.* 50:58-75, 1932.
- Bodansky, M. Production of hypoglycemia in experimental derangements of the liver. *Am. J. Physiol.* 66:375-379, 1923.
- Idem. Effect of chloroform and phosphorus poisoning on carbohydrate tolerance. *Biol. Chem.* 58:515-522, 1923.
- Conn, J. W., Newburgh, L. H., Johnson, M. W., and Sheldon, J. M. Study of the deranged carbohydrate metabolism in chronic infectious hepatitis. *Arch. Int. Med.* 62:765-787, 1938.
- Nadler, W. H., and Woller, J. A. Hepatogen C hypoglycemia associated with primary liver cell carcinoma. *Arch. Int. Med.* 44:700-710, 1929.
- Joseph, H. Spontaneous hypoglycemia in childhood. *Am. J. Dis. Child.* 38:46-757, 1929.
- Judd, E. S., Kepler, E. J., and Rysnerman, E. H. Spontaneous hypoglycemia report of two cases associated with fatty metamorphosis of the liver. *Am. J. Surg.* 24:345-363, 1934.
- Soskin, S., and Mirsky, I. A. The influence of progressive toxic liver damage upon the dextrose tolerance curve. *Am. J. Physiol.* 122:649-656, 1935.
- Althausen, T. L., and Stockholm, M. Deposition of glycogen in normal and in experimentally damaged livers after oral and intravenous administration of dextrose. *Am. J. Digest. Dis. & Nutrition* 4:752-758, 1938.
- Soskin, S., and Hyman, M. Physiological basis of intravenous dextrose therapy for diseases of the liver. *Arch. Int. Med.* 64:1265-1270, 1939.
- Jones, C. M. The treatment of acute hepatic insufficiency and its relation to prognosis. *Am. J. Digest. Dis. & Nutrition* 3:624-629, 1936.
- Ravdin, I. S., Rhoads, J. E., Frazier, W. D., and Ulin, A. W. The effect of recent advances in biliary physiology on the mortality following operation for common duct obstruction. *Surgery* 3:805-814, 1938.
- Ravdin, I. S. The protection of the liver from injury. *Surgery* 8:204-211, 1940.
- Snell, A. M. The treatment of liver disease. *Ann. Int. Med.* 12:592-608, 1938.
- Althausen, T. L. Dextrose therapy in diseases of the liver. *J. A. M. A.* 100:1163-1167, 1933.
- Müller, L. E., and Whipple, G. H. Chloroform liver injury increases as protein stores decrease: studies in nitrogen metabolism in these dogs. *Am. J. M. Sc.* 199:204-216, 1940.
- Messinger, W. J., and Hawkins, W. B. Arsenphenamine liver injury modified by diet, protein and carbohydrate protective but fat injurious. *Am. J. M. Sc.* 199:216-225, 1940.
- Johnson, J., Ravdin, I. S., Vars, H. M., and Zintel, H. A. Symposium on preoperative and postoperative treatment: effect of diet on composition of the liver in the presence of obstruction of the common bile duct. *Arch. Surg.* 40:1104-1115, 1940.
- Brues, A. M., Drury, D. R., and Brues, M. C. A quantitative study of cell growth in regenerating liver. *Arch. Path.* 22:658-673, 1936.
- Moore, T. S., and Smith, A. H. Diet and tissue growth: the regeneration of liver tissue on various adequate diets. *J. Exper. Med.* 40:13-23, 1924.
- Beit, C. H., Ferguson, G. C., and Hershey, J. M. Choline and liver fat in diabetic dogs. *J. Physiol.* 79:94-102, 1933.
- Beit, C. H., and Huntman, M. E. The effects of the components of lecithine upon deposition of fat in the liver. *J. Physiol.* 75:405-412, 1932.
- Channon, H. J., and Wilkinson, H. Protein and the dietary production of fatty livers. *Biochem. J.* 29:350-355, 1935.
- Dragstedt, L. R., Van Prohsaka, J., and Harms, H. P. Observations on a substance in pancreas (a fat metabolizing hormone) which permits survival and prevents liver changes in depancreatized dogs. *Am. J. Physiol.* 117:175-181, 1936.
- MacKay, E. M. The influence of pancreas extract (a fat metabolizing hormone) upon fat deposition in the liver on a low protein diet. *Am. J. Physiol.* 119:783-786, 1937.
- Beit, C. H., and Ridout, J. H. The pancreas and the deposition of fat in the liver. *Am. J. Physiol.* 122:67-72, 1938.
- Dragstedt, L. R. The present status of lipocase. *J. A. M. A.* 114:29-32, 1940.
- Addis, T., Poo, L. J., Lew, W., and Yuen, D. W. Gravimetric methods for the determination of total body protein and organ protein. *J. Biol. Chem.* 113:497-504, 1936.
- Lew, W. L. Liver proteins: the question of protein storage. *J. Biol. Chem.* 115:491-510, 1936.
- Whipple, G. H. Protein production and exchange in the body, including hemoglobin, plasma protein and cell protein. *Am. J. M. Sc.* 126:609-621, 1938.
- Kerr, W. J., Hurwitz, S. H., and Whipple, G. H. Regeneration of blood serum proteins. I. Influence of fasting upon curve of protein regeneration following plasma depletion. *Am. J. Physiol.* 47:356-369, 1918.
- Idem. Regeneration of blood serum proteins. III. Liver injury alone. *Am. J. Physiol.* 47:379-392, 1918.
- Erickson, C. C., Heckel, G. P., and Knutti, R. E. Blood plasma proteins as influenced by liver injury induced by carbon tetrachloride and gum acacia. *Am. J. Path.* 14:537-556, 1938.
- Myer, W. L., and Keen, C. S. Relation of plasma proteins to ascites and edema in cirrhosis of the liver. *Arch. Int. Med.* 55:349-359, 1935.
- Turner, H., and Backus, H. L. The clinical significance of serum proteins in hepatic diseases compared with over liver function tests. *Am. J. M. Sc.* 193:788-801, 1937.
- Foley, E. F., Keeton, R. W., Kendrick, A. B., and Darling, D. Alterations of serum protein as an index of hepatic failure. *Arch. Int. Med.* 60:64-76, 1937.
- Peters, J. P., and Euseman, A. J. The serum proteins in diseases not primarily affecting the cardiovascular system or kidneys. *Am. J. M. Sc.* 186:603-633, 1933.
- Butt, H. R., Snell, A. M., and Keys, A. Plasma protein in hepatic disease: study of colloid osmotic pressure of blood serum and of ascitic fluid in various diseases of the liver. *Arch. Int. Med.* 63:143-155, 1939.
- Mann, F. C. The role of the liver as the commissariat of the body. *Am. J. Digest. Dis. & Nutrition* 4:355-364, 1937.
- Gorgy, P., and Goldblatt, H. Hepatic injury on a nutritional basis in rats. *J. Exper. Med.* 70:185-192, 1939.
- Neale, R. C., and Winter, H. C. Identification of active crystalline substance from the liver which protects against liver damage due to chloroform or carbon tetrachloride and study of related compounds. *J. Pharmacol. & Exper. Therap.* 62:127-148, 1938.
- Ruch, A. R., and Hamilton, D. The experimental production of cirrhosis of the liver by means of a deficient diet. *Bull. Johns Hopkins Hosp.* 66:185-198, 1940.
- Moore, T. Vitamin A and carotene, the vitamin A reserve of the animal human being in health and disease. *Biochem. J.* 31:155-164, 1937.
- Stewart, J. D., and Rourke, G. M. unpublished data.
- Breese, B. B., and McCoord, A. B. Vitamin A absorption in catarrhal jaundice. *J. Pediatr.* 16:139-145, 1940.
- Greaves, J. D., and Schmidt, C. L. A. The role played by bile in the absorption of vitamin D in the rat. *J. Biol. Chem.* 102:101-112, 1933.
- McNally, R. W., Shapiro, P., and Melnick, P. The effect of viosterol in jaundice. *Surg. Gynec. & Obst.* 60:785-801, 1935.
- Stewart, J. D., and Rourke, G. M. Control of prothrombin deficiency in obstructive jaundice by use of vitamin K. *J. A. M. A.* 113:2223-2227, 1939.
- Patek, A. J., Jr. Treatment of alcoholic cirrhosis of the liver with high vitamin therapy. *Proc. Soc. Exper. Biol. & Med.* 37:329-1937.
- Annus, I. W., and Comfort, M. W. Portal cirrhosis with good immediate results from medical treatment: presentation of case. *Proc. Staff Meet. Mayo Clin.* 13:435-438, 1938.
- Wintrobe, M. M. Relation of disease of the liver to anemia: type of anemia response to treatment and relation of type of anemia. *Arch.*

65 Rod

sweet

66. Dat

he and

67. Idem

9 1273

1285 1935

68. Schönheyder, F.: The quantitative determination of vitamin K. *Biochem. J.* 30:890-896, 1936.
69. Almquist, H. J., and Stokstad, E. L. R.: Hemorrhagic chick disease of dietary origin. *J. Biol. Chem.* 111:105-113, 1935.
70. Quick, A. J.; Stanley-Brown, M., and Bancroft, F. W.: A study of the coagulation defect in hemophilia and in jaundice. *Am. J. M. Sc.* 190:501-511, 1935.
71. Warner, E. D.; Brinkhous, K. M., and Smith, H. P.: A quantitative study on blood clotting: prothrombin fluctuations under experimental conditions. *Am. J. Physiol.* 114:667-675, 1936.
72. Stewart, J. D., and Rourke, G. M.: Prothrombin and vitamin K therapy. *New Eng. J. Med.* 221:403-407, 1939.
73. Butt, H. R.; Snell, A. M., and Osterberg, A. E.: The use of vitamin K and bile in the treatment of hemorrhagic diathesis in cases of jaundice. *Proc. Staff Meet., Mayo Clin.* 13:74-80, 1938.
74. Snell, A. M.: Vitamin K: its properties, distribution and clinical importance: preliminary report. *J. A. M. A.* 112:1457-1459, 1939.
75. Doisy, E. A.; Binkley, S. B.; Thayer, S. A., and McKee, R. W.: Vitamin K. *Science* 91:58-62, 1940.
76. Butt, H. R.; Snell, A. M.; Osterberg, A. E., and Bollman, J. L.: Treatment of hypoprothrombinemia: use of various synthetic compounds exhibiting antihemorrhagic activity (vitamin K₁ activity). *Proc. Staff Meet., Mayo Clin.* 15:69-73, 1940.
77. Ansbacher, S.; Fernholz, E., and Dolliver, M. A.: Vitamin K-active derivatives of 2-methyl-1, 4-naphthoquinone. *J. Am. Chem. Soc.* 62:155-158, 1940.
78. Stewart, J. D.: Oral and parenteral use of synthetic vitamin K-active substances in hypoprothrombinemia. *Surgery* (in press).
79. Youmans, J. B.: The present status of vitamin deficiencies in practice. *J. A. M. A.* 108:15-20, 1937.
80. McEster, J. S.: Borderline states of nutritive failure. *J. A. M. A.* 112:2110-2114, 1939.
81. Carr, F. H., and Price, E. A.: Colour reactions attributed to vitamin A. *Biochem. J.* 20:496-501, 1926.
82. Josephs, H. W.: Studies in vitamin A: relation of vitamin A and carotene to serum lipids. *Bull. Johns Hopkins Hosp.* 65:112-124, 1939.
83. May, C. D.; Blackfan, K. D.; McCreary, J. F., and Allen, F. H., Jr.: Clinical studies of vitamin A in infants and in children. *Am. J. Dis. Child.* 59:1167-1184, 1940.
84. Jeans, P. C.; Blanchard, E., and Zentmire, Z.: Dark adaptation and vitamin K: new photometric technic. *J. A. M. A.* 108:451-458, 1937.
85. Steininger, G.; Roberts, L. J., and Brenner, S.: Vitamin A in the blood of normal adults: the effect of a depletion diet on blood values and biophotometric readings. *J. A. M. A.* 113:2381-2387, 1939.
86. Goodhart, R. S., and Sinclair, H. M.: Estimation of cocarboxylase (vitamin B₁ diphosphate ester) in blood. *Biochem. J.* 33:1099-1108, 1939.
87. *Idem*: Deficiency of vitamin B₁ in man as determined by the blood cocarboxylase. *J. Biol. Chem.* 132:11-21, 1940.
88. Melnick, D., and Field, H., Jr.: Chemical determination, stability and form of thiamin in urine. *J. Biol. Chem.* 130:97-107, 1939.
89. Robinson, W. D.; Melnick, D., and Field, H., Jr.: Urinary excretion of thiamin in clinical cases and the value of such analyses in the diagnosis of thiamin deficiency. *J. Clin. Investigation* 19:399-408, 1940.
90. Ferrebee, J. W.: The urinary excretion of riboflavin: fluorometric methods for its estimation. *J. Clin. Investigation* 19:251-256, 1940.
91. Spies, T. D.; Ladisch, R. K., and Bean, W. B.: Vitamin B₆ (pyridoxin) deficiency in human beings. *J. A. M. A.* 115:839, 1940.
92. Farmer, C. J., and Abt, A. F.: Ascorbic acid content of blood. *Proc. Soc. Exper. Biol. & Med.* 32:1625-1629, 1935.
93. Quick, A. J.: The nature of the bleeding in jaundice. *J. A. M. A.* 110:1658-1662, 1938.
94. Brown, P. W.: Adequate vitamin dosage. *Proc. Staff Meet., Mayo Clin.* 15:215-217, 1940.
95. Coffey, R. J.; Mann, F. C., and Bollman, J. L.: The effect of the exclusion of bile on the absorption of foodstuffs. *Am. J. Digest. Dis. & Nutrition* 7:143, 1940.
96. Albright, F., and Stewart, J. D.: Hypovitaminosis of all fat-soluble vitamins due to steatorrhea. *New Eng. J. Med.* 223:239-241, 1940.
97. Ivy, A. C., and Berman, A. L.: The rationale of bile salt therapy in biliary tract disease. *Minnesota Med.* 22:815-820, 1939.
98. Greene, C. H.; Walters, W., and Frederickson, C. H.: The composition of the bile following the relief of biliary obstruction. *J. Clin. Investigation* 9:295-310, 1930.
99. Bollman, J. L., and Mann, F. C.: The influence of the liver in the formation and destruction of bile salts. *Am. J. Physiol.* 116:214-224, 1936.
100. Jungner, G.; Rydin, A., and Josephson, B.: Elimination of cholic acids. II. In experimental jaundice. *Acta med. Scandinav.* 97:254-264, 1938.
101. Stewart, H. L., and Cantarow, A.: Renal lesions following the injection of sodium dehydrocholate in animals with and without biliary stasis. *Arch. Path.* 20:866-881, 1935.
102. Lamson, P. D.: The part played by the liver in the regulation of blood volume and red corpuscle concentration in acute physiological conditions. *J. Pharmacol. & Exper. Therap.* 16:125-134, 1920.
103. Adolph, E. F.; Gerbasi, M. J., and Lepore, M. J.: Redistributions of water following transfusions and infusions. *Am. J. Physiol.* 107:647-666, 1934.
104. Crandall, L. A., Jr., and Roberts, G. M.: Blood volume after intravenous fluid in normal and Eck fistula dogs. *Am. J. Physiol.* 101:24, 1932.
105. Skelton, H.: The storage of water by various tissues of the body. *Arch. Int. Med.* 40:140-152, 1927.
106. Crandall, L. A., Jr., and Roberts, G. M.: Increased water exchange following Eck fistula in dogs. *Am. J. Physiol.* 117:318-322, 1936.
107. Soffer, L. J.; Dantes, D. A., and Sobotka, H.: Electrolytes of blood and urine of dogs with acute hepatic injury produced by arsphenamine. *Arch. Int. Med.* 60:509-521, 1937.
108. Jones, C. M., and Eaton, F. B.: The prognostic significance of a spontaneous diuresis in acute or subacute disease of the liver. *New Eng. J. Med.* 213:907-918, 1935.
109. Boyce, F. F., and McFetridge, E. M.: So-called "liver death": clinical and experimental study. *Arch. Surg.* 31:105-136, 1935.
110. Elsom, K. A.: Renal function in obstructive jaundice. *Arch. Int. Med.* 60:1028-1033, 1937.
111. Ayer, D.: Renal lesions associated with deep jaundice: with comments on their relations to those in the so-called hepatorenal syndrome and in transfusion reactions. *Arch. Path.* 30:26-41, 1940.

CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITALANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 26521

PRESENTATION OF CASE

A fifty-six-year-old man entered the hospital complaining of pain in his chest.

Seven weeks before admission, after drinking ice water, the patient suddenly developed a pain in his left chest anteriorly that was aggravated by breathing and accompanied by shortness of breath, general malaise and weakness. In addition, a dry cough, which he had had for many years, produced a moderate amount of purulent sputum. These symptoms persisted, though the pain became intermittent, and two weeks before admission he was forced to stop work and remain in bed. The temperature for these two weeks averaged 100.2°F., the cough increased and the sputum though never copious was most marked at night and in the morning. He had lost 7 pounds since the onset of his symptoms and had suffered from moderately severe frontal headaches.

On examination the patient was well-developed and well-nourished but appeared acutely and chronically ill, showed evidence of recent weight loss and was slightly dyspneic. He coughed frequently bringing up small amounts of rusty tenacious sputum. Numerous angiomas were present over the chest and abdomen, and on the right buttock there was a 5-cm. reddened area covered with numerous small pustules. Expansion of the left chest was limited, and in its mid-portion there was dullness to percussion both anteriorly and posteriorly. Over this area were many fine and coarse moist rales with suppression of the breath sounds, which had a slight tubular quality. Occasional rales were heard at the right apex. There was no tracheal shift. Examination of the heart was negative. The liver was firm and nontender and extended three fingerbreadths below the costal margin in the right mid-clavicular line. The fundi showed moderate arteriosclerosis with clear disks and no hemorrhage or exudate. Examination of the nervous system was negative.

The temperature was 101°F., the pulse 95, and the respirations 35.

Examination of the urine was negative. Examination of the blood showed a red-cell count of 5,000,000 with a hemoglobin of 75 per cent, and

a white-cell count of 38,000 of which 89 per cent were polymorphonuclears. Blood cultures on two occasions were negative. The nonprotein nitrogen of the blood serum was 16 mg. per 100 cc., the chlorides 94.8 milliequiv. per liter and the carbon dioxide combining power 26.3 milliequiv. Sputum cultures grew *Staphylococcus albus*, alpha hemolytic streptococci, and on one occasion a few colonies of beta hemolytic streptococci. No pneumococci were isolated by culture or the mouse method, and no tubercle bacilli or fungi were found in smears. The tuberculin test was negative in a dilution of 1:40,000 on two occasions.

Fluoroscopic examination of the chest showed movement in both diaphragms. There was a small amount of fluid in the left costophrenic angle posteriorly. The process on the left side involved practically the whole left upper lobe and consisted of areas of diffuse density alternating with small round aerated spaces, some of which had the appearance of small cavities. There was no evidence of respiratory shift of the mediastinum, and the left main bronchus was completely visible. In the right-upper-lung field there were lines of increased density with some mottling, particularly in the infraclavicular area.

An electrocardiographic recording showed normal rhythm with a rate of 100. The PR interval was questionably 0.20 second (marked somatic tremor), and there was low voltage of the QRS complex in Leads 1, 2 and 3.

On the sixth hospital day a bronchoscopic examination was performed. The abnormal findings were limited to the left bronchial tree, where there was considerable reddening of the mucosa of the medial wall of the main bronchus. The left-upper-lobe orifice was not seen, due to angulation. The bronchoscope passed well into the left-lower-lobe bronchus, which showed reddening with a moderate amount of secretion. There was no outcropping, and the terminals were normal. The patient continued to run a spiking temperature up to 104°F., and two weeks after admission developed auricular fibrillation, which was controlled by digitalis. Sulfapyridine was given, but stopped because of distressing vomiting. Sulfathiazole also produced vomiting and, in addition, a nonpruritic maculopapular rash over the forearms, backs of the hands, face and lower abdomen. Both the sulfathiazole and ammonium chloride, which the patient had been receiving for his cough, were discontinued, and the rash disappeared in two days. The former was again instituted two days later in half dosage (3 gm. daily), but the skin eruption reappeared. Three weeks after admission the patient became dis-

orientated. A neurological examination was negative. X-ray study of the chest at this time showed no change in the process. Four weeks after admission bronchoscopic examination was repeated. Considerable secretion was found in the trachea, and several cubic centimeters of thick greyish-white purulent material was aspirated. The right main bronchus showed mucosal injection, and coughing expelled purulent secretion from each bronchial subdivision. There was no localized change in the bronchial mucous membrane. On entering the left main bronchus, the lumen was obstructed just inside the carina by what appeared to be inflammatory swelling. The mucous membrane was engorged and injected, and the bronchoscope could not be introduced more than 0.5 cm. into the bronchus.

At about this time, the patient developed an extensive, partially confluent, papular, erythematous eruption over the entire body except the palms, soles and mucous membranes. The consensus leaned toward a septic origin from pulmonary disease rather than dermatitis medicamentosa. Two months after admission a thoracentesis was performed through the eighth left interspace in the posterior axillary line, and 650 cc. of clear, amber fluid withdrawn. At this point the patient complained of pain, so that the procedure was terminated, although the fluid was still running freely. That evening after a mild attack of dyspnea he coughed up a small amount of bright-red blood and later approximately 150 cc. of blood clot; he then became pulseless and died immediately. During the two months of hospitalization the white-cell count showed a gradual decline from the initial figure of 38,000 to 9900.

DIFFERENTIAL DIAGNOSIS

DR. FREDERICK T. LORD: May we see the x-rays?

DR. AUBREY O. HAMPTON: These films were taken at intervals over a period of not quite one month. In the anteroposterior view it seems as if the whole left lung were diseased, but in the lateral it is apparent that only the left upper lobe is involved. It is honeycombed with cavities but in spite of this is not appreciably reduced in size. The interlobar septum between the upper and lower lobes on the left is straight and in about its normal position. In the films taken a few days later the left side of the diaphragm is higher and there appears to be reduction in the size of the left lung.

In the final film, taken twenty-two days later, a great change is evident. The patient was evidently examined in the upright position. Most of the left chest appears to be occupied by fluid

and air with a definite fluid level between them, simulating a hydrothorax or pyopneumothorax. However, the upper margin of the air bubble is at the third rib posteriorly, and it definitely does not reach the apex of the pleural cavity.

DR. LORD: Is this after tapping?

DR. DONALD S. KING: No, before tapping.

DR. LORD: From the examination of the chest, there is little to be added to the information obtained from the x-ray examination. There were rales at the right apex, and in confirmation the films show definite mottling in the upper part of the right-lung field extending fairly well out to the periphery. There was an enlarged liver and some arteriosclerosis. There was lowering of the nonprotein nitrogen and chlorides in the blood. There were negative tests with tuberculin on two occasions. Of two bronchoscopies, the first was negative and the second, three weeks later, showed obstruction of the left main bronchus.

We should like to know more about certain matters. Was there a history of hemoptysis, or of foul odor to the sputum? It would be desirable to have further information about the pleural fluid, that is, the specific gravity, the cellular formula and the results of cultures, guinea-pig inoculation and search for tumor cells.

The abnormal features of the blood chemistry may be ascribed to the disturbances arising in consequence of the present illness.

The negative tests on two occasions with a 1:40,000 dilution of tuberculin are of doubtful significance. Though the use of highly diluted tuberculin has been advocated as a diagnostic test, its value as a measure of activity of a tuberculous process has not been established, and the use of a high dilution in such a case as this is subject to the disadvantage that patients in an advanced stage of the disease are likely to fail to respond to the test. I do not know the margin of error in the routine reliance on a negative test with a dilution of 1:40,000, but it must be considerable. In Ayman's* investigation of 82 patients with active tuberculosis, only 69 per cent gave positive reactions (10 by 9 mm. or more in size) with 0.1 cc. of a 1:50,000 dilution of old tuberculin.

In the use of tuberculin for diagnosis, it is customary to use stronger solutions. In the screening of school children in Massachusetts with tuberculin, a single test is made with 0.1 cc. of a 1:10,000 dilution of old tuberculin. There is, however, a small margin of error unless those who fail to react to this dose are tested with stronger solutions. When the conditions are more favorable and with the patient under observation in a

*Ayman, D.: The intracutaneous quantitative tuberculin test. *J. A. M. A.* 103:154-157, 1934.

hospital, the first dose, except in cases in which unusual sensitivity is to be expected, may well be 0.01 mg (0.1 cc. of a 1:10,000 dilution), and if there is no reaction to this amount, 0.1 mg is used as the second dose, followed by 1.0 mg if the second test is negative.

To come back to the differential diagnosis, it is evident that the patient had some arteriosclerosis. There was arteriosclerotic heart disease. The enlargement of the liver may have been due to chronic passive congestion or cancer. It is obvious that he had a bronchopulmonary suppurative process with probable cavitation. Whether the cavitation was due to lung destruction or bronchiectasis cannot be determined without the use of Lipiodol, but that substance was not employed in this case.

To return to the effusion, passive congestion as a cause may be excluded. It may have been of inflammatory (tuberculous or nontuberculous) or malignant origin, and the evidence does not permit a decision between these possibilities.

The most interesting, and probably the most important, aspect of the problem is the explanation of the mass in the left primary bronchus. A biopsy of this mass might have established the diagnosis. We have to consider two possibilities. The commonest cause of bronchial obstruction, excluding tenacious secretion, is inflammation. Although the bronchoscopist thought it was of inflammatory origin, it must be admitted that he could not tell by inspection alone. There may be evidence of inflammation at the surface on inspection and even under the microscope, and yet there may be an underlying cancer. It is a question whether carcinoma would grow with sufficient speed to appear within a period of three weeks, the interval between the two biopsies, but the possibility may be granted for a rapidly growing neoplasm. There is also the possibility that the mass is tuberculous, and the x-ray appearance of the right apex suggesting tuberculosis lends some support to this hypothesis. The failure to find tubercle bacilli in the sputum is against it, but we should like to know how many specimens of sputum were examined.

There is another interesting matter in respect to the manner of this patient's death. The immediate cause of death seems to have been hemorrhage into the air passages. He coughed up 150 cc. of blood clot and died immediately, probably from asphyxia.

In respect to diagnoses, we can be certain of bronchopulmonary suppuration with cavitation, probably secondary to bronchial occlusion. So far as the nature of the bronchial mass is concerned,

I should regard it as either inflammatory or malignant and confess that I cannot make the decision between these possibilities.

DR KING: We saw the patient and followed him along in the Thoracic Clinic. We thought at first that he had an oat cell carcinoma, but we could not prove it. Then we began to think of a primary suppurative process but could not identify the organism. We simply did not have a diagnosis when he died. I am still interested in knowing whether you think that is pyopneumothorax or a large cavity in the left apex.

DR LORD: That the gas bubble did not reach the apex suggests the possibility that the fluid was in the lung or encysted in the pleura. Six hundred cubic centimeters of clear fluid would, however, be a large amount to be obtained from the lung unless a cyst of the lung were tapped.

DR LOWREY F. DAVENPORT: Perhaps I was negligent in not taking a biopsy specimen at the time of the second bronchoscopy. This man was in wretched condition, and I thought at the time that to do so was unwise.

DR FRANCIS T. HUNTER: I remember this patient well. I might mention something not emphasized in the printed sheet, that is, the character and amount of the sputum. After they put him on postural drainage, he drained an enormous amount of sputum, probably the most tenacious sticky material I have ever seen, with no odor and no organisms, although at one time we found large numbers of branching mycelium. The sputum had been standing around in a warm room, and the mycelium was never found again; we consequently discounted it.

CLINICAL DIAGNOSIS

Pulmonary sepsis?
Carcinoma of lung?

DR LORD'S DIAGNOSES

Arteriosclerosis
Arteriosclerotic heart disease.
Bronchopulmonary suppuration (? lung abscess or bronchiectasis).
Bronchial mass (? inflammatory or malignant)
Hemorrhage into the air passages.

ANATOMICAL DIAGNOSES

Bronchiogenic epidermoid carcinoma, left upper lobe.
Lung abscess (? monilia)is)
Pulmonary hemorrhage.
Chronic fibrous pleuritis.
Encapsulated hydrothorax.
Empysematous blebs, right upper lobe.
Arteriosclerosis, moderate, coronary and aortic.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: At autopsy the left pleural cavity was almost completely obliterated by fibrous adhesions. Between the adhesions were various encapsulated cysts containing straw-colored fluid. It must have been one of these that had been tapped. The left upper lobe was virtually replaced by a multilocular abscess cavity into which several bronchi opened. In the wall of one of the bronchi a small mass was found, and a frozen section was made in which no tumor could be recognized, so that the death certificate was signed as pulmonary abscess. When the regular microscopic sections came through, it was apparent that the little nodule was, after all, an epidermoid carcinoma, not much over a centimeter in diameter; but it was large enough to have obstructed the bronchus, and the remainder of the findings were all secondary to it. The cavity at the time of autopsy was almost completely filled with blood, which also plugged the rest of the bronchial tree, as Dr. Lord suggested. A small mass of inspissated secretion, which was found in the cavity along with the blood clot, was sectioned and found to consist of a practically pure mass of mycelium. I therefore think that yeast infection was probably the cause of the abscess.

A PHYSICIAN: What about the mottling of the right apex?

DR. MALLORY: There were a number of emphysematous blebs and a few old fibrous scars but no active tuberculous process.

DR. WYMAN RICHARDSON: Was the brain examined?

DR. MALLORY: No.

The liver was large and showed chronic passive congestion. The heart was very slightly enlarged and showed a moderate amount of coronary disease.

DR. DAVENPORT: What was the relation of the mass to the bronchi? Was it possible to have reached it through the bronchus?

DR. KING: I am quite sure that it could not have been reached.

CASE 26522

PRESENTATION OF CASE

A seventy-three-year-old engineer entered the hospital for investigation of an unexplained fever.

Because of the patient's physical and mental condition, the history was obtained from his wife, who had been with him constantly. Six weeks before admission the patient complained of general malaise and shortly afterward had a severe chill. Two days later he was lethargic and somnolent,

and that night had another severe chill followed by profuse sweating, which soaked the bedclothes. The next day he was completely exhausted, feverish, continually perspiring and had one slight chill. For the next two weeks he ran a constant temperature of 99 to 102°F., and at the end of that time entered another hospital, where physical examination and laboratory investigations were unfruitful; the white-cell count on several occasions was 6000, and the only positive findings were a dry, furry tongue and a constant, spiking temperature. During the next three weeks the patient became confused, complained of soreness in his head and had one momentary attack of dizziness, but his temperature decreased slightly. One week before admission he was given Neoprontosil and shortly afterward became pale and delirious, with tachycardia and a barely perceptible pulse. The drug was withdrawn for two days and then re-instituted, with similar though less severe results. During this week before admission, the patient became lethargic and often delirious, and the nurse stated that he had visual and auditory hallucinations, but answered questions rationally. In addition there was incontinence of urine and, on one occasion, of feces. He had lost 50 pounds since the beginning of his illness.

Several years before admission the patient had had two skin lesions, one situated under the knee, the other near the shoulder. These were slightly reddened, rough, irregular, raised blotches, which healed with an ointment. About two years before admission he complained of a feeling of "sour gas" regurgitating into his esophagus after meals. This complaint was investigated at another hospital, where a gastrointestinal series and barium enema were negative. He was treated successfully by a change in diet.

The patient had had typhoid inoculations on two occasions, the last eight years before admission. He had always lived in Maine, except for short visits to the West Indies. The family history was noncontributory.

On examination the patient was well-developed and well-nourished, flushed, perspiring freely and appeared acutely ill. Numerous 2-mm. tan spots were present over the trunk. Rales were heard at both lung bases. Examination of the heart was negative; the blood pressure was 110 systolic, 66 diastolic. The abdomen was negative to palpation, but the spleen was enlarged to percussion. Examination of the nervous system was negative.

The temperature was 101.5°F., the pulse 104, and respirations 36.

Examination of the urine showed a +++ test for albumin and rare hyaline and granular casts.

Examination of the blood showed a red-cell count of 3,880,000 with a hemoglobin of 115 gm. (photoelectric-cell technic), and a white cell count of 17,600, of which 96 per cent were polymorphonuclears, 2 per cent lymphocytes and 2 per cent monocytes. Blood cultures and a blood Hinton test were negative. The sedimentation rate was 59 mm. in one hour. Agglutination reactions were positive up to dilutions of 1.80 for typhoid bacilli and 1:160 for paratyphoid B bacilli, but were negative in all dilutions for paratyphoid A bacilli. The nonprotein nitrogen of the blood serum was 28 mg per 100 cc, the blood sugar 188 mg. Examination of the stools was negative, and no pathogens were present.

X-ray examination of the esophagus with barium revealed displacement of the esophagus to the right just above the arch of the aorta and displacement of the entire lower portion to the left, with no evidence of obstruction or involvement of the esophageal wall. There was definite enlargement of the mediastinal lymph nodes, particularly on the right side. An area of mottled density, which was present in the right costophrenic angle, corresponded to the general shape and position of a partially calcified middle lobe. The diaphragm was high on both sides, and the upper portion of the right lung was a little more radiant than the left. There was no mediastinal shift. Films taken in another hospital two weeks before admission showed practically the same findings. X-ray examination of the abdomen showed what appeared to be an enlarged spleen. The liver did not appear to be enlarged, and the visible bones were normal.

The patient developed a brassy cough and signs of respiratory obstruction. His fever continued, ranging between 101 and 103.5°F. He was given sulfanilamide, one 500 cc. transfusion, and two x-ray treatments of 50 r each to the mediastinal mass. Despite these measures the patient died on the sixth hospital day.

DIFFERENTIAL DIAGNOSIS

DR LOWREY F. DAVENPORT We have to discuss the case of a seventy-three-year-old man whose outstanding symptom at the time of admission was unexplained fever. The onset with a chill makes us think in the beginning of some acute infectious process starting abruptly. Apparently that was also the thought of those treating him at the other hospital, because blood cultures were taken, and although they were negative, he was treated with Neoprontosil. In a man of seventy-three with this degree of fever, we might reason-

ably expect the mental confusion described in the record prior to admission here.

What is helpful in the past history? What clues are we given? We are told that he had always lived in Maine, except for visits to the West Indies. That brings up the question of some type of obscure infection that occurs in semitropical regions. He had two negative blood cultures. Agglutination tests were equivocal. We are told that he had been inoculated twice previously with typhoid vaccine and we know that during any infectious process the titer of a Widal agglutination test does go up. The fact that it was weakly positive for both typhoid and paratyphoid B bacilli makes us dismiss typhoid fever as a possibility.

On examination at entry, the patient was obviously ill, in respiratory distress, and running a high fever. Certain additional data on physical examination seem to be significant. They were the enlarged spleen and the numerous pigmented areas over the body. The person taking the history must have been impressed with the pigmentation. He obtained from the wife a story of two earlier skin lesions, one on the leg and one near the shoulder. They appear to have healed quite promptly, and I believe that we can dismiss them.

I am prepared at this point to exclude typhoid fever. We have two positive blood cultures that would tend to exclude, but not necessarily, other acute bacteremic processes. There is nothing in the physical examination to indicate a hidden focus of sepsis to explain this fever. So at this point let us have the benefit of the x-ray evidence.

DR GEORGE W. HOLMES I presume that these films were taken with the patient lying down. This would account to some extent for the high sharply domed diaphragm. But the diaphragm is rather high even for a patient in the prone position, the right side especially. The mediastinal shadow is certainly increased to the right, and the aorta displaced toward the left. From the character of the mass we should expect that it represented lymph nodes. It is stated in the fluoroscopic note that the esophagus was also displaced, suggesting that the mass was in the region of the peribronchial nodes. In the region of the middle lobe, there is increased density, and when films were taken with the Bucky diaphragm, areas that suggest calcification became apparent. In some of the films there is a suggestion that the upper portion of the right lung is unusually bright as compared with the left side. That would be additional evidence that there was some collapse of the middle lobe with an overdistention of the

The New England Journal of Medicine

Formerly the
Boston Medical and Surgical Journal

Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE
ON PUBLICATIONS

Official Organ of
THE MASSACHUSETTS MEDICAL SOCIETY
THE NEW HAMPSHIRE MEDICAL SOCIETY
THE VERMONT STATE MEDICAL SOCIETY

EDITORIAL BOARD

Joseph Garland, M.D.	John P. Sutherland, M.D.
William B. Breed, M.D.	Stephen Rushmore, M.D.
George R. Minot, M.D.	Henry R. Viets, M.D.
Frank H. Lahey, M.D.	Robert M. Green, M.D.
Shields Warren, M.D.	Charles C. Lund, M.D.
George L. Tobey, Jr., M.D.	John F. Fulton, M.D.
C. Guy Lane, M.D.	A. Warren Stearns, M.D.
William A. Rogers, M.D.	Dwight O'Hara, M.D.

ASSOCIATE EDITORS

Thomas H. Lanman, M.D.	Donald Munro, M.D.
Henry Jackson, Jr., M.D.	

Walter P. Bowers, M.D., EDITOR EMERITUS

Robert N. Nye, M.D., MANAGING EDITOR

Clara D. Davies, ASSISTANT EDITOR

SUBSCRIPTION TERMS \$6.00 per year in advance, postage paid, for the United States; Canada, \$7.04 per year; \$8.52 per year for all foreign countries belonging to the Postal Union.

MATERIAL for early publication should be received not later than noon on Saturday.

THE JOURNAL does not hold itself responsible for statements made by any contributor.

COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston, Massachusetts.

THE MEDICAL CARE OF THE SICK IN THEIR HOMES

In 1795, Boston, within whose "harbour there is room enough for near 500 sail to lie at anchor, and in good water too," boasted of some 18,000 inhabitants, and within that year Dr. John Fleet, first district physician to the Boston Dispensary visited 80 patients in their homes—patients too ill to leave their beds, yet too poor to be able to afford a private physician. Since then the work of the Boston Dispensary, established to "provide medical advice and relief to the sick poor," has increased and multiplied and prospered until in 1939 its "family physicians" made 54,500 house visits on over 30,000 patients.*

Many of Boston's leading physicians of the older

generation look back on their district work as one of the most valuable experiences of their early professional careers. Many a Tufts medical student of today has, under the aegis of the New England Medical Center, in a similar role gained valuable bedside experience, and under the guidance of a district physician has given timely care to those whose need was great.

Thus Boston, unlike other cities of the country, has profited by the services of a privately supported medical charity. Through the years, however, it became increasingly necessary to appeal to the city government for financial aid, and with the probable dwindling of voluntary philanthropic contributions it is indeed questionable whether such a service can be supported, even in part, by private charity.

If the Boston Dispensary and other agencies concerned are to be relieved by the City of Boston of the financial burden of domiciliary medical care, the question remains as to how best the work may be carried on. Many suggestions have been made, but there is a preponderance of opinion that, for Boston, the ideal arrangement would be through a contractual agreement between the city and the Boston Dispensary whereby the poor might be assured of service of the high level that has been maintained for many years.

Whatever the eventual outcome may be, it is apparent that the problem of domiciliary medical care of the indigent sick is of great importance, and that it deserves the careful consideration of all concerned.

SKI PATROLS ON TRAILS AND SLOPES

THIS winter, between three and five million people are expected to participate in skiing. With the tremendous growth in the popularity of the sport, many serious and minor accidents have occurred on the trails, principally because so many novices were attempting feats beyond their skill and endurance. The number of injuries has been reduced by the efforts of the voluntary patrols maintained by almost every ski club in the country. The American Red Cross has helped standardize the first-aid methods, rescue practice and trans-

*Wing, F. E.: *Medical Care of the Sick in Their Homes*. 31 pp. Boston: The Boston Dispensary, 1940.

portation equipment, the principles of which are contained in its booklet, *Ski Safety and First Aid*

During the coming season, the members of the patrols plan to emphasize the prevention of accidents, but, as in previous years, they will also be on the alert to help the injured. On many popular trails the Red Cross and some ski clubs have established caches in which blankets, toboggans, heating pads and other necessary equipment are kept ready for emergencies.

First aid procedure involves considerable skill and diligence. The loaded toboggan must be maneuvered slowly and carefully down the trail, so that the injured person may not be in danger of further hurt, might may come before an ambulance reaches the sufferer, blankets and splints must be brought back from the hospital, equipment must be returned to the cache for further need, and dressings and bandages must be replaced.

The work of preventing accidents and administering first aid is done in the holiday time of the patrol members, who forego their own recreational skiing and make long, tedious and often dangerous trips to assist skiers in distress. In many sections the patrols cover all slopes and trails at the end of the day to be sure that nobody has been left on a mountain with an injury or broken equipment.

To promote safety in skiing, the patrols direct beginners to practice slopes, where they may receive instruction before attempting the more difficult and dangerous trails. Both novices and experienced skiers are cautioned not to start down a steep slope unless they know how to slow down and stop. By wearing goggles while climbing, the skier may avoid extremely painful and often serious snow blindness. Beginners are instructed to stay close to the side of the trail when climbing, to slow down when rounding blind turns and to travel in groups and remain together. They are also told to observe snow conditions and are warned that the cold weather aggravates injuries that under different circumstances might be slight.

This increased interest in skiing is a sign of progress — so far as the general health of the peo-

ple is concerned — in an age when the use of automobiles has largely eliminated walking as an exercise, furthermore, these efforts of the American Red Cross and the ski clubs to prevent accidents and to render adequate first aid treatment deserve proper recognition.

MEDICAL EPONYM

TETRALOGY OF FALLOT

This syndrome was described by Arthur Fallot in a series of papers, entitled *Contribution à l'anatomie pathologique de la maladie bleue (cyanose cardiaque)* [Contribution to the Pathologic Anatomy of the Blue Sickness (Cardiac Cyanosis)], which appeared in *Marseille Medical* (25: 77-93, 138-158, 207-223, 270-286, 341-354 and 403-420, 1888).

A portion of the translation (page 419) follows:

The blue sickness, especially when diagnosed in the adult, is the result of a small number of perfectly definite cardiac malformations.

Of these cardiac malformations, one exceeds all the others in frequency, since we have found it in nearly 74 per cent of our cases.

This malformation is a true anatomicopathological entity, represented by the following tetralogy: stenosis of the pulmonary artery, communication between the ventricles, displacement to the right of the origin of the aorta and hypertrophy of the right ventricle, almost always concentric in type. To these may occasionally be added, with only accessory significance, a persistent ductus Botalli.

R W B

MASSACHUSETTS MEDICAL SOCIETY

RESOLUTION ON THE DEATH OF DR. EDWARD J. DAILEY

WHEREAS, An old wise Father has seen fit to call from among our midst our friend and colleague, Dr. Edward J. Dailey, and

WHEREAS, This tragic death, which makes us pause and reflect on the uncertainties of life, brings a realization of how great a loss the profession has sustained by his untimely death, be it therefore

RESOLVED, That in the death of Dr. Edward J. Dailey, a long, active and useful career has been brought to a close. We mourn his loss as a brother physician, as a loyal citizen and as a genial friend. And be it further

RESOLVED, That these resolutions be published in the *New England Journal of Medicine* and the *Somerville Press*, placed on records of the society,

hemorrhage be withheld from young patients in good condition until the clot has become fairly firm, and that during recovery such therapy be carried out freely. Dr. Cutler approved of this regimen and added that few people die of hemorrhage from natural causes if left alone.

The second case, presented by the surgical staff, was that of an elderly woman who entered in an aphasic state with incomplete history of abdominal pain of forty-eight hours' duration. There had been no bowel movements; only fluids could be tolerated by mouth. The past history was relevant in that an adenocarcinoma of the uterine fundus was diagnosed in 1923, and was treated first by roentgen rays and by panhysterectomy in 1926, when residual disease was still found on diagnostic dilatation and curettage. Physical examination revealed that the patient was slightly dehydrated, with slight right-lower-quadrant tenderness, occasional audible peristalsis, a questionable prepubic mass, and some tenderness but no mass on rectal examination. The blood pressure was 170 systolic, 90 diastolic, and there was a slight apical systolic murmur. The significant laboratory data were a leukocyte count of 17,700 with 84 per cent neutrophils, an erythrocyte count of 5,500,000, a hemoglobin content of 90 per cent and a very slight trace of albumin in the urine. After parenteral fluids were started, flat plates of the abdomen were taken, and the patient was removed to the operating room, where an exploratory laparotomy was performed. The peritoneal cavity contained 250 cc. of blood-tinged fluid, and there were distended loops of reddish-blue ileum. Adhesive bands were severed, and the patient was returned to the ward on Wangenstein drainage. The following day the white-cell count was 15,500, and the red-cell count 4,500,000 with 80 per cent hemoglobin. Blood chlorides were 106 milliequiv., and plasma proteins 6 gm. per 100 cc. The case was presented to illustrate another form of shock and its treatment.

The speaker of the evening was Dr. John Scudder, of Columbia University, whose subject was "Shock: Blood studies as a guide to therapy." In his introduction, Dr. Scudder pointed out that these studies considered shock from the aspect of individual cells and their metabolism. Original studies by Dr. Osterhout on certain unicellular plant cells demonstrated that a concentration gradient exists between the intracellular and extracellular components. Trauma of any sort was shown to cause a breakdown of the barrier, with an escape of the predominant intracellular ion, potassium, and a transfer of sodium in the opposite direction. In *Nitella*, increasing the concentration of potassium in pond water is measurably changed in the action current.

In mammals, such as the cat, by merely changing the concentration of potassium of the blood, one is able to bring about various changes, visible by the electrocardiograph, that lead to ventricular fibrillation, asystole and death. The administration of sodium salt, by causing a diuresis of the potassium, will bring these electrocardiographic changes back to normal, provided therapy has been instituted early.

That the same fundamental phenomena occur in human shock was demonstrated by the increase of potassium following a ruptured kidney and in untreated burns. Further observations revealed that there was a measurable increase of the specific gravity of the peripheral blood, although the hematocrit reading and other routine laboratory data remained unchanged. Dr. Scudder urged that the therapy of shock cases be based, therefore, on the hematocrit reading, the specific gravity of the whole blood and plasma, and the plasma protein, rather than on changes of blood pressure or ionic concentration, which occur only later.

The speaker then discussed the background and the methods employed at his clinic for carrying out these determinations easily and practically. The need for performing all four tests, rather than any single one, was emphasized, and this was illustrated by cases of shock wherein the hematocrit reading or the plasma protein, or both, remained well within normal limits despite a dangerous degree of shock. Dr. Scudder pointed out that an adequate level of protein is an aid against dangerous shock. Decrease in plasma proteins is usually found in severe cases of burns, combined with great hemoconcentration. This is a situation difficult to combat and should be treated by the injection of plasma rather than of whole blood.

The speaker demonstrated the ingenious apparatus whereby the specific gravity of whole blood and plasma may be simply and accurately determined by an application of Stokes' law of falling bodies. A measured drop of the appropriate fluid is put in a tube and the speed of its descent timed with a stopwatch and compared with that of a fluid of known specific gravity. Then the utilization of the linear relation between the plasma protein content and the plasma specific gravity, originally suggested by van Slyke, allows the former value to be computed readily.

Dr. Scudder asserted that an intelligent appraisal of these four determinations results in an accurate and rapid appreciation of the underlying pathologic physiology in cases of shock and thus leads to the early adoption of the appropriate line of therapy to be employed. The speaker himself was first interested in these studies following his experience with Asiatic cholera epidemics in India. The mortality drop from 80 to 20 per cent during the last century has resulted through intelligent use of proper fluids.

Physiologic saline solution is often of advantage early in cases of shock to correct dehydration and the ionic equilibrium before blood transfusion is employed. Dr. Scudder again reminded the group of the great lowering of the plasma protein in burns as contrasted with hemorrhage and of the great advantages of using infusions of plasma instead of whole blood in the former condition.

He pointed out that some patients who fail to respond properly to intravenous saline may continue to have increasing hemoconcentration. The use of adrenocortical extract in such cases has proved to be a corrective measure in both animals and man. It was suggested that there was a premature breakdown of the sympathicoadrenal mechanism in these rare cases.

Finally Dr. Scudder briefly discussed the problems involved in preserving and using reserve blood. Studies have revealed that there is a gradual loss of leukocytes, particularly polymorphonuclear neutrophils, whereas the erythrocytes and the hemoglobin content remain essentially unchanged. A small loss of cell volume is associated with a diminution of potassium. It was therefore suggested that as small an interface as possible be employed in storage flasks to decrease the possibility of ionic loss. Withdrawal of blood under carbon dioxide was found beneficial, and sodium citrate was thought the best anticoagulant.

Plasma is drawn off after one week and has been found beneficial in practical experience. As was pointed out, this was to be expected as the result of electrophoretic charts, wherein plasma more nearly approaches blood than any other fluid. Lyophilic serum was shown to fall down in this respect, and it was said that its use has not proved practical. Plasma, mixed with equal parts of saline, has proved very beneficial in surgical emergencies.

The discussion was opened by Dr. S. J. G. Nayak, of the

ston City Hospital, who reported on cross-perfusion experiments that appeared to show that there is no circulatory breakdown substance responsible for shock. Dr Stead marked that medical shock may often be observed when there is no disproportion between the existing vascular flow and the circulating blood volume. Therefore there may be no change of any of the factors used as routine criteria of shock. On the other hand, he has been impressed by the amount of change in the blood constituents that may occur without shock. He cited cases with plasma protein levels that rose from 68 to 80 gm per 100 cc.

Dr J E Dunphy stated that the characteristic clinical picture of shock usually appears when treatment is no longer of avail. Therapy must be instituted early, particularly in cases of peritonitis, intestinal obstruction and so forth, which are now seen more commonly than in the past due to trauma or burns. And it is particularly here that Dr Scudder's procedures allow accurate fluid therapy.

Dr Dunphy has been impressed, however, with the need for clinical as well as laboratory judgment, for example, when the protein value may appear normal initially but may need supporting when hemoconcentration has been overcome.

In conclusion, Dr Scudder introduced the problem of adrenocortical extract sometimes exerts a deleterious effect, particularly in peritonitis. He suggested as a possible mechanism the action of this extract in suppressing potassium content, as shown by Loeb. Desoxycorticosterone may cause a fall from 50 to 25 milliequivalents, with diastolic standstill. And this effect is even more serious in peritonitis, in which the potassium value often reaches levels of 3 milliequivalents.

NOTICES

BOSTON DOCTORS' SYMPHONY ORCHESTRA



The Boston Doctors' Symphony Orchestra will rehearse under Alexander Thiede, formerly concert master of the Cleveland Symphony Orchestra, every Thursday at 8:30 p.m. Those interested in becoming members should communicate with Dr Julius Loman, Pelham Hall Hotel, Brookline (BEA 2430).

unicate with Dr Julius Loman, Pelham Hall Hotel, Brookline (BEA 2430)

NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held in the classroom of the Nurses' Residence on Thursday evening, January 2, at 7:15 p.m. Dr Perry Pittman will be chairman.

PROGRAM

Electrocardiographic and Roentgenologic Evidence of Heart Disease with Demonstration of the Stethoscaphic. Drs Merry Pittman and Bianca R. Lia.

MASSACHUSETTS DEPARTMENT OF CIVIL SERVICE AND REGISTRATION

Medical Inspector of Schools, Health Department, \$836.57 a Year, Fall River

Director of State Civil Service, Ulysses J. Lupien, has announced that competitive examinations are to be held

on January 18 to find eligibles for appointment to the position of medical inspector of schools, Health Department, Fall River.

The entrance requirement is as follows: applicants must be registered physicians under the Massachusetts Board of Registration in Medicine. The subjects and weights of the examination are as follows: training and experience, 2; practical questions, 3; total, 5. Applicants must obtain a grade of 70 per cent in each subject in order to become eligible. The last date for filing applications is January 4, at 12:00 noon.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING SUNDAY, DECEMBER 29

MONDAY DECEMBER 30
12:15-1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

TUESDAY DECEMBER 31
12:15-1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

DECEMBER 27—Waltham Medical Meeting. Page 1039, issue of December 19.

DECEMBER 27—Danvers State Hospital clinicopathological conference. Page 999, issue of December 12.

DECEMBER 27-29—National Convention of the Association of Medical Students. Boston.

JANUARY 2—New England Hospital for Women and Children. Noted above.

JANUARY 3—Massachusetts Memorial Hospitals staff meeting. Page 999, issue of December 12.

JANUARY 4—American Board of Obstetrics and Gynecology. Page 787, issue of November 7.

JANUARY 5-MARCH 2—Public Health Lectures. Cambridge Hospital. Page 1039, issue of December 19.

JANUARY 7—Greater Boston Medical Society. Page 1039, issue of December 19.

JANUARY 9—Pentucket Association of Physicians. Page 263, issue of August 15.

JANUARY 13-14—Third Annual Congress on Industrial Health. Page 999, issue of December 12.

FEBRUARY 20-22—American Orthopsychiatric Association, Inc. Page 999, issue of December 12.

MARCH 8—American Board of Ophthalmology. Page 201, issue of August 1.

MARCH 12-14—New England Hospital Assembly. Hotel Statler, Boston.

APRIL 21-25—American College of Physicians. Page 1065, issue of June 20.

MAY 21-22—Massachusetts Medical Society. Boston.

JUNE 2-6—American Medical Association. Cleveland, Ohio.

DISTRICT MEDICAL SOCIETIES

ESSEX SOUTH

JANUARY 8—Visceral Pain Its relief. Dr James C. White. Danvers State Hospital Hathorne.

FEBRUARY 5—Gastric and Duodenal Ulcer. Diagnosis and treatment. Dr Arthur Allen. Lynn Hospital.

MARCH 5—X-ray in Heart Disease. Dr Merrill C. Sosman. Essex Sanatorium, Middleton.

APRIL 2—Pediatric Problems in General Practice. Dr Joseph Garland. Addison Gilbert Hospital, Gloucester.

MAY 14—Relation of the Doctor to the Law. Mr Leland Powers. New Ocean House, Swampscott.

FRANKLIN

JANUARY 14

MARCH 11

MAY 13

Meetings will be held at 11 a.m. at the Franklin County Hospital, Greenfield.

NORFOLK

JANUARY 28—Orney Hospital.

FEBRUARY 25—Medicolegal meeting. 8:30 p.m. Hotel Puritan, Boston.

MARCH 25—To be announced.

MAY 8—Centors meeting. Hotel Puritan.

SUFFOLK

JANUARY 29 — Page 604, issue of October 10.

APRIL 30 — Page 604, issue of October 10.

WORCESTER

JANUARY 8 — Worcester City Hospital, Worcester.

FEBRUARY 12 — Worcester State Hospital, Worcester.

MARCH 12 — Memorial Hospital, Worcester.

APRIL 9 — Hahnemann Hospital, Worcester.

Supper at 6:30 p.m. followed by a business meeting and scientific program.

BOOK REVIEWS

Dermatologic Therapy in General Practice. By Marion B. Sulzberger, M.D., and Jack Wolf, M.D. 8°, cloth, 680 pp., with 65 illustrations and 25 tables. Chicago: Year Book Publishers, Inc. \$4.50.

This work is the answer to the long-existing need for an intelligible, complete and concise compendium of procedures to be followed in the majority of skin diseases that are encountered by physicians in general practice. The dermatologist can also gain some profit from almost every page in the book. Although practically every procedure described and every preparation and prescription discussed can be found in the general literature, to collect them in a handy form would require an extensive search of the dermatological texts and journals. The work suffers somewhat, however, from an inconsistent mixture of unofficial abbreviations of Latin and English, all mixed together in the same prescription—a fault that occurs quite frequently in many textbooks. Since most prescriptions are written in Latin with proper endings, they all should have been written in the same manner. However, the very extensive formulary and the minutiae of nursing and of the technic of treatment, as given in this book, leave very little to be desired.

The first two chapters are the essence of the book, so far as the general practitioner is concerned; they contain a thorough discussion of the principles of external medication. In the chapter on urticaria, there are an excellent condensation of diet tables and a general description of allergic conditions of the skin. There are over fifty pages of description and detailed instruction for the diagnosis and treatment of fungus infections. The various charts and tables and the outline form of presentation, as well as the pertinent photographs, are valuable features of the book. Even the busiest general practitioner will greatly benefit by reading this very admirable contribution to the practical management of dermatoses.

The Diagnosis and Treatment of Diseases of the Peripheral Arteries. By Saul S. Samuels, A.M., M.D. Second edition. 8°, cloth, 372 pp., with 106 illustrations. London: Oxford University Press, 1940. \$6.50.

In this second edition, Dr. Samuels attempts to bring the subject of peripheral arterial disease up to date. The book considers mainly thromboangiitis obliterans and arteriosclerosis. In the former disease, the author still relies largely on treatment with intravenous hypertonic salt solution, and he is content to wait several weeks or months for spontaneous separation of gangrenous parts. All physicians will not agree with his stated policy of never amputating in this disorder. More physicians will, however, be in accord with his emphasis of general hygiene and abstention from smoking.

Although the book presumes to be comprehensive, the sections on disorders other than Buerger's disease and arteriosclerosis are too brief and sketchy to be of much value. The chapter on Raynaud's disease is particularly

disappointing, since diagnostic and operative procedures are but briefly mentioned.

Some of the subject matter in the book is actually leading. Uroselectan is mentioned as a painless material for arteriography; in the reviewer's experience, this is of the most irritating solutions available. The advocacy of hot baths and diathermy in organic arterial disease may be justified by his experience, but he makes no mention of recent observations on the rapid disintegration of ischemic tissue in the presence of a heated environment.

It seems advisable to sound a note of caution and specify what patients should be treated in this manner. The emphasis on instrumental measurement rather than palpation of the pulses seems most unfortunate. On page 31, the author states, "palpation of the posterior tibial artery is notoriously unreliable," and again on page 28, "in a crude way, digital palpation of peripheral arteries may give some clue concerning the condition of the circulation." Finally, the tone of the book is much too dogmatic for a subject that to a great extent is still controversial. The book seems to extend but little beyond the knowledge of vascular disorders.

Adventures of a Biologist. By J. B. S. Haldane. Second edition. 8°, cloth, 281 pp. New York and London: Harper & Brothers, 1940. \$2.75.

Professor Haldane, a distinguished scientist, a materialist and a Marxist, takes the reader behind the scenes and let him know what sort of questions interest the scientist. He draws attention not only to the unsolved but also to the unasked problems. His essays, by-products of scientific teaching and research, cover a broad field ranging from discussions on weather, earth and sun to life, race, heredity, death, philosophy and politics. The point is emphasized throughout that man is a machine but at the same time an individual, so that life becomes an extraordinary bundle of contradictions. A warning is given against harnessing biology to the car of any political party. On the other hand the author is strongly of the opinion that scientists should take an active part in politics, since the questions asked in the biological sphere will depend on our economic and political orientation. This is a book that may be recommended without reservations.

A Text-book of Psychiatry for Students and Practitioners. By D. K. Henderson, M.D. (Edin.), F.R.F.P.S. (Glas.), F.R.C.P.E., and R. D. Gillespie, M.D. (Glas.), F.R.C.P. (Lond.), D.P.M. (Lond.). Fifth edition. 8°, cloth, 660 pp. London: Oxford University Press, 1940. \$6.00.

This edition of a standard and good textbook of psychiatry, designed for the use of students and practitioners, is clearly written and fairly comprehensive. It has an important, new chapter on the psychiatry of childhood. There is also a relevant and clear outline of the relation of psychiatry to law. It is not doctrinaire, for it neither rejects nor accepts the various schools which have elaborated theories, especially concerning the functional mental states. There is a good section on the use of insulin and Metrazol, although, unfortunately, the use of convulsive and shock therapy for the depressive and involuntic states, where the greatest benefit from these methods seems indicated by present-day experience, is not discussed.

In the present unsatisfactory state of psychiatry, so far as classification, pathology and treatment are concerned, this book is as good as any for the beginner in this difficult field.

